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NEW ENGLAND, NEUROSURGERY AND THE NEUROSURGEON*

WILLIAM JASON MIXTER, M.D.†

BOSTON

MANY authors have written of the beginnings of medicine in New England, and through their writings we find something of the foundation on which medicine in this corner of the United States was built. We read of the minister-physician and the barber-surgeon in the early days of our colony. The minister-physicians were among the leading men of their respective communities. Theirs was no easy job. They had souls to save as well as lives. Let us not cavil if their theology breathed of hell-fire and brimstone and if the purge was the most frequently employed form of medication. What if they did "breathe a vein" for almost any ailment, and what if the barber-surgeon did use all sorts of curious and revolting things for dressings? Those were the days of angleworm oil, of nanny tea and other archaic medicaments. Some benighted peoples still use curious forms of treatment. Bear's gall bladders, not many years ago, had a ready sale to the Chinese doctors of the Pacific Coast. We can say, "Oh, yes, the Chinese"—but we had quaint customs here at home. I can remember removing a poultice from a carbuncle in my early days—an amateur poultice, to be sure. It was offensive to the nose and to the eye and proved to be a large chew of tobacco.

These early members of our fraternity had learned their medicine in England, but when they came to America they left behind much of the quackery and charlatanism that was rife in England during the fifteenth and sixteenth centuries. Remember that this was a new country and that life was cheap and the way of life was hard. They were pioneers and they cut out the nonessentials.

We read of starvation, of Indian raids, of the various epidemics that decimated the colonies. The worst of their plagues was smallpox, that dread scourge, that stalked through the settlements in more deadly fashion than an Indian war party. Smallpox took its toll of lives time after time until Zabdiel Boylston, about 1720, read or heard of direct inoculation with smallpox material. He must have been a courageous man, this Boston physician, for he decided to use this new and almost untried method of disease prevention. Many powdered heads were shaken in disapproval, but the experiment was a success. It is an interesting fact that his records of these cases were excellent. His statistics proved the value of inoculation, and his work was accepted here and abroad.

During these years from the establishment of the colonies to Zabdiel Boylston's time we find certain changes in the practice of our profession. The physician continued to be one of the leading spirits of the community. He was prominent politically, but he no longer played the dual role of medical adviser and minister to the soul. We find that medical thought was still dominated by the teachings in vogue in Great Britain, but we find each prominent physician teaching his apprentice or group of apprentices, and also find that many of these young men went to England to complete their education. A few went farther and studied on the Continent. They were independent in medical thought as they were in their politics. They delved into new things in medicine as they explored the terra incognita that lay beyond their settlements. They were still pioneers.

We read of those gallant gentlemen who gave of themselves that these United States should be forever free—names like Warren that have come down from father to son or nephew and still abide on the roster of the Massachusetts Medical Society. We read also of the Loyalists who, devoted to King and mother country, followed the English troops—exiles for their political convictions. We may read between the lines and learn that the doctor of those early days was far more a leader in his community than we are—a man of broad education and interests, looked up to and admired for his good works and his knowledge. There must have been much of sorrow

*The Annual Discourse delivered at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1940.

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and much of bitterness in 1776, for we read that some of the pupils of the beloved teacher, James Lloyd, sailed for Halifax to lead the lonely lives of exiles. Other pupils, the younger and more radical element, donned the blue and buff of the colonial forces. The doctor's life was a hard one. He stood on his own feet, foursquare to the world, and worked out his problems for himself. He had no assistance from laboratory and roentgen ray and all those things that make diagnosis easier for us.

About the turn of the century, while the states were settling down trying to find out what they had won besides independence, the character of medical education changed. Schools were established and the apprentice system was abolished except for postgraduate education. We looked to England for much of our medical lore, but we as a pioneer community developed our own trends in medicine. That word "pioneer" means much in American life. We can be proud that the members of our profession lived up to their traditions and to the trend of their own times. Untrammeled by the taboos of European medicine, they developed along their own lines.

Many tall tales have come down to us of these old days before 1846, when Morton soaked a sponge with ether that the grand old man of the Massachusetts General Hospital, John Collins Warren, might demonstrate that painless surgery had arrived.

Even the small-town doctor did his investigating, and under difficulties that would make us cringe. There are two treasured legends in my own family, one concerning my great-great-grandfather, Ingalls Kittredge. He practiced in Beverly, and it is said he brushed up his anatomy as occasion offered. One rainy night he crossed the bridge which then, as now, connected Beverly and Salem and drove his shay by devious ways to Peabody, where he met certain grave robbers who delivered to him the body of a recently deceased and, we hope, respected citizen of that rather lonely hamlet. On his way home after midnight with the subject seated beside him, he reached the bridge. The toll gate was open and all was dark. A cut with his whip and the horse galloped out on the bridge. Just before he reached the gate the keeper rushed out and slammed it shut. The sudden stop unseated the doctor's gloomy companion, who pitched forward and nearly went out over the wheel.

Old Ingalls Kittredge must have had a strong and dexterous hand as well as an agile brain. He grasped him by the nape of the neck and pulled him back. "Sit down, ye drunken fool!" was his comment. He paid his toll and drove home. Can we not take this legend to heart? Even if the night is dark and stormy and the way to our goal long, can we not forge ahead to the increase of our own knowledge and the betterment of our service to our fellow men?

Ingalls Kittredge, his son, also was of an investigative turn of mind. One day he had as a patient a man dying with fever. There was a mass in the right side of the abdomen. He decided there was pus present, and to the horror of his associates he cut into the abscess, washed it with clean water from the spring and drained it with clean tow from the center of the bundle. The man lived, else I might not be here, for the good townspeople of Beverly beset his house at the corner of Essex and Federal Streets with a hangman's rope at hand until it was known the patient was out of danger.

So much for the past. We can see a change — a tendency toward specialization if you will — even from the earliest days of the Massachusetts Bay Colony. At first our predecessors combined medicine with political and religious leadership. By the time of the Revolution they had given up their pastoral activities; then other intellectuals gradually assumed political leadership — medicine is a jealous mistress and will not permit a divided allegiance.

Our heritage, together with that of our predecessors in the last hundred years, is a grand one: self-confidence, leadership, the spirit of the pioneer, coupled with the desire to investigate and the will to achieve. They carried it with them in the migration to the West in the eighteen-forties and fifties, those hardy men of New England. From one of them, an obscure army surgeon at Mackinaw, came the brilliant investigation of gastric secretion that made the name of Beaumont famous. It was not only the adventurers who made the trek across the mountains to the plains. Whole families went, and to one of these pioneer groups that settled on the southern shore of Lake Erie we shall turn later for the greatest of the pioneers in neurosurgery — Harvey Cushing.

Neurosurgery has its beginnings in the cloudy past, before the days of history. This is attested by a collection of Peruvian skulls — one of the treasures of the Warren Museum at the Harvard Medical School. It is interesting to learn that then as now the man with the investigative mind might find that someone else had the same thought. In the museum at Copenhagen last summer I saw skulls from the Scandinavian countries with the same four saw cuts, the same holes, made to let out the evil spirit, and in some of them, as in the Peruvian skulls, the patient had survived the ordeal, for new bone had formed around the edge

of the opening. It is interesting to realize that in all ages and among all people the brain has been known as the seat of consciousness. I suppose that Cain learned this scientific truth when he struck Abel; that is, if he hit him on the head. It is even more interesting to realize the depths of our own ignorance of consciousness, the cause of sleep and so forth. We still have many things to learn. However, that is not the point at the moment. The point is that the priest, the surgeon or someone has been opening the skull since before the dawn of history, probably with the idea of curing some mental ill.

Neurosurgery in America can be said to be the offspring, born in lawful wedlock, of neurology and general surgery, with physiology as godfather. It is difficult to state exactly when and where this interesting event took place.

It seems to me that the organization in Philadelphia during the Civil War of an army hospital devoted to the treatment of nervous diseases, both medical and surgical, marks the beginning of the special handling of neurosurgical cases. The men in charge of this project were well suited to carry out the new venture. S. Weir Mitchell was a neurologist and a physiologist, W. W. Keen an enthusiastic and daring surgeon, while George Moorehouse was an able medical man and administrator. The surgical cases treated were almost entirely due to injuries of peripheral nerves. Today neurosurgery is far more engaged with the central nervous system than with somatic nerve fibers outside the cerebrospinal axis.

By 1888 cranial localization and the surgery of tumors had become an important subject for consideration. Reading the transactions of the first meeting of the Congress of Physicians and Surgeons held at Washington in September of that year, we find the record of a symposium devoted to these subjects. Keen and Roswell Park, who were surgeons, took part, as did Charles K. Mills, M. Allen Starr and others, who were neurologists. David Ferrier and Sir Victor Horsley, leaders in physiology and brain surgery, came from England to attend this meeting, and here we see again the close association of American and British medicine. We find also in these transactions the mention of a case of brain damage caused by birth injury reported by William N. Bullard in the February 16, 1888, issue of the *Boston Medical and Surgical Journal;* the operation was performed by Edward H. Bradford.

Let us think a moment of how neurosurgery was handled in Boston at that time and for the next twenty-five years. James Jackson Putnam had been appointed "electrician" to the Massachusetts General Hospital in 1872 and neurologist in 1873. Since that time neurology had progressed, but we find mention of barely a dozen cases of brain tumor in the programs of the Boston Society of Psychiatry and Neurology before 1905. Neurosurgical operations were few and far between, and were performed by the general surgeons at the instigation of and under the direction of the neurologists. However, even then certain surgeons were picked out, or perhaps picked on, by the neurologists to be the operators. As we have seen in the earlier reports, Bradford was one. My father was another. His was an investigative spirit and he delighted in exploring new fields. He obtained from Stone and Webster, then a young electrical engineering concern, a small electric motor, and devised a guarded circular saw with flexible cable which he used to open the skull. I keep the motor and saw as a memento of those early days. We must remember that all surgeons of that day here and abroad had ingrained in them by their predecessors the lesson that one of the prime requisites of surgery was speed. My father had it. Horsley had it. Maurice Richardson had it. With it they combined great deftness and precision. Speed is of great value today, but not so valuable as it was then, for now we have all the modern devices to combat shock and hemorrhage, and anesthesia has become a high art.

I can remember many of those early cranial operations during my work as house officer at the Massachusetts General Hospital, which began in 1906. The commonest was the operation for trigeminal neuralgia — usually the Abbe type, with intracranial section of the second and third divisions of the fifth cranial nerve. My father modified this operation by plugging the foramens with silver amalgam and later with bone wax. I can remember operations for tumor — one in particular, on a patient of Dr. Putnam's, about 1908. We operated in a private hospital on Commonwealth Avenue, and Dr. Putnam's office nurse had never seen a brain operation. She stood between the windows of the room, and as the first incision in the scalp was made and the old T-shaped hemostats were applied, she collapsed on the floor with her head in the basin in which the bloody sponges were dropping. Someone dragged her out, and that was that.

I also remember etherizing while Maurice Richardson operated for cerebellar tumor — big, red-faced, with a rolling gait accentuated by an old Potts fracture, he was a splendid general surgeon. There was no head rest. The anesthetist held the patient's head with one hand and the cone with the other, and the orderly or someone else poured on ether when the cone was held out under the edge of the sheet. I nearly drowned and nearly

etherized myself, and had to have a shampoo afterward. My own first attempts at brain surgery were of the same sort. I followed my masters. Their work was good as measured by the surgery of that day. I assisted Horsley in London for three months. Speed was his fetish. A sweeping scalp incision, four saw cuts with a hand saw, three or four taps of mallet on chisel, and a square of bone leaped out. Then came a rapid enucleation and even more rapid closure, all under a stream of weak bichloride solution. A physiologist, a neurologist, a surgeon, all in one, but trained in the old school of surgery.

What of neurosurgery in Massachusetts beyond the few men I have mentioned? Edward H. Nichols and Frederick C. Lund at the Boston City Hospital and others were doing neurosurgery as it came along. At the Massachusetts General Hospital, Charles A. Porter was working with Walter E. Paul, the neurologist, on peripheral nerve injuries and getting quite a series of cases. Not one of these men considered neurosurgery even as his major interest. The neurologists were doing more than the surgeons, for they were truly specializing in their chosen field and pioneering in the diagnosis of neurosurgical conditions and in some instances in treatment. Others besides Putnam were at work. I learned to know and respect Philip C. Knapp and E. Wyllys Taylor for their studies on the brain. Paul, as stated above, was working on the peripheral nerves, and George L. Walton had already published his important paper on cervical dislocations. I have one of the reprints which the latter gave to my father. Were any one of us to write that paper today there is little that we could add to it except some roentgen-ray pictures.

But at this time Harvey Cushing in Baltimore, Charles L. Frazier in Philadelphia and Ernest Sachs in St. Louis were beginning to develop real neurosurgical clinics. Cushing in particular was limiting his work to neurosurgery and modifying the meticulous, painstaking surgical technic originated by Halsted. Brain surgery requires the utmost in gentle handling of tissues, exact hemostasis and the persistence and ability to carry on for hours if necessary. To achieve this end, one must have a surgical team that is near perfection and every aid in anesthesia, instruments and operating-room facilities that modern science can give. Cushing recognized this fact and also the importance of exact and painstaking localization, with the use of every aid to be obtained from neurology and physiology.

Harvey Cushing came to Boston to become Moseley Professor of Surgery at Harvard and to thrill the world with the till then undreamed possibilities of cranial surgery. To Cushing, Massachusetts owes its supremacy in neurosurgery for many years. To him came patients from all over the world, and the young men flocked to sit at his feet and learn of his art. For with him, neurosurgery became an art. Surgeon, neurologist, pathologist and physiologist, he combined them all. Let us honor with the highest praise this illustrious figure in our profession who so recently has gone from us.

Let us examine the changes in neurosurgery that the seventy-five years from that first war hospital in Philadelphia to the present time have brought.

The pioneers have led us on from small beginnings to great achievements. Peripheral nerve surgery has become standardized. The surgery of brain tumor is on a firm foundation, and the spinal cord, the pituitary gland, even the ventricles of the brain, are open to inspection and treatment if need be.

What has Massachusetts added to the score since Harvey Cushing gave impetus to neurosurgery in this community?

A neurosurgical service is now an important part of many of our large hospitals. Donald Munro, the son of a gifted surgeon, John C. Munro, has taught us much about skull fracture, and also to seek out and find that elusive and treacherous aftermath of head injury, the subdural hematoma. Gilbert Horrax is following Cushing's lead in the surgery of brain tumor. Tracy J. Putnam left Boston last fall to become the head of the Neurological Institute in New York City. There he is carrying on the brilliant research work that he began in Boston. At New Haven, William German and John Fulton are carrying on the Cushing tradition of investigation and brilliant technical achievement. They received their training here in Massachusetts and as New Englanders we can claim them as our own. At the Massachusetts General Hospital we are busy with our problems in relation to the central nervous system. From a few scattered beds neurology and neurosurgery have grown to the status of independent services with a permanent visiting staff and a group of residents. From less than fifty operative procedures a year we have grown to more than that number a month. In the surgery of the sympathetic nervous system James C. White and Reginald H. Smithwick are exploring untrodden pathways.

The specialist does not spring full panoplied as Pallas Athena did from the head of Zeus. His is a long apprenticeship; not to one teacher as in colonial days, but nonetheless an apprenticeship. He must sweat his way through college and medical school with the others who, like himself, be

lieve that the healing art is the ultimate in service to humanity. Then comes his hospital service, his work in allied branches of medicine and finally his residency in his chosen field. Five full years and perhaps more. Then comes the plunge and he is out on his own.

Cushing's clinic at the Peter Bent Brigham Hospital was the first in New England to educate neurosurgeons, and they are following in his footsteps all over the world. Now there are other groups carrying out the same plan. We find these young men in medical schools in large centers and also in the small cities. Some of them have had hard work to get started, owing to professional jealousy and the desire of some of our profession to do everything in surgery whether they do it well or ill. More have been welcomed as helpers in the field and through their efforts the standards of practice in their communities are being elevated. I look forward to the day when the whole of this country will be covered by men trained in this branch of surgery as it is by the exponents of the other specialties.

Prophecy is dangerous and the prophet is often discredited, but I believe that we can see a bit ahead. The malignant gliomas still defeat us. It is for some new pioneer to lead us out of that hornet's nest. The sympathetic nervous system has yielded many triumphs since Royle's ill-starred attempts to modify spasticity brought it to our attention. Fulton at the Peter Bent Brigham Hospital studied one of these early cases and was quick to see the possibilities of its effect on the vascular system. Smithwick and White have added to our knowledge, and I believe there are great possibilities ahead, including control of pain, the amelioration of hypertension and so forth.

The possibility of the surgical treatment of certain forms of insanity is more than a rainbow. Destructive surgery, it is true, but nevertheless it may be the dawn of a new era in the treatment of this tremendous group of sufferers.

Neurosurgery is ever changing. As it goes forward to these new things, it is setting aside and giving to the profession at large certain things that it called its own not so many years ago. Who does the nerve sutures in our great hospitals today? Not the neurosurgeons: no, indeed. The house officer dealing with severed tendons in the wrist picks up and sutures the median or ulnar nerve as a matter of course. The surgeon caring for a fracture of the humerus cares for the musculospiral nerve, and in the war hospitals of Europe the operating surgeons in the mobile units are repairing bullet wounds of nerves and of the central nervous system.

What lesson may we learn from these facts which I have brought so sketchily to your attention? Neurosurgery has been and is undergoing a period of growth and expansion, partly on account of research and advance by neurosurgeons in their own field, and partly because of the application in neurosurgery of advances in general surgery, in neurology and in physiology. It is by reason of this continuing advance that neurosurgery is accepted as a specialty in medicine. It is not a narrow, hidebound specialty, but a broad specialty equipped and able to invade that all-important cavity containing the central nervous system and to follow through the body wherever nerve cells send their tendrils. But that is not all. Today the neurosurgeon is going forward as a pioneer, following the precept of all pioneers and blazing out new trails for others to follow. So it is with all specialization in medicine. Specialties will hold unto themselves certain procedures which, because of their inherent difficulties or because of the complicated equipment necessary to carry them out, are not suitable for general use. It would be folly for one not especially trained to attempt the surgery of brain tumor, nor could one of us neurosurgeons in his own office perform the miracles of diagnosis carried out daily by the radiologist. As soon as a procedure becomes standardized and can be applied by the profession at large, it should cease to be held and guarded as a potboiler by the specialist. If he waits beside the trail, nursing his little potboiling fire, he will fall behind his brother pioneers and the profession may lack something which they could use for the betterment of humanity.

These are the thoughts that I would leave with you in these closing hours of the 1940 meeting of the Massachusetts Medical Society. All of us are seekers after truth, and especially for that truth which will benefit the health of our fellow men. Ours is a science, an art and not a business. To apply business methods to medicine either by our own volition or by legislation will impede its advance. By giving of ourselves without stint we shall obviate the necessity of such regulation. Surgery is like a great river ever flowing onward. This river is made up of the waters of many streams, and of these neurosurgery is one. Each stream contributes something to the whole and to the smooth course of the river's progress. Any one of us, in practice, in the laboratory, in a specialty or in any of the many branches of medical science, may come upon some hidden spring to add to its volume. Let us, as members of the Massachusetts Medical Society, seek out these hidden springs and share them with the brethren of our profession, to the end that suffering and sickness be lessened in the world.

319 Longwood Avenue.

MINOR CAUSALGIA: A HYPERESTHETIC NEUROVASCULAR SYNDROME*

JOHN HOMANS, M.D.

BOSTON

THERE is a very peculiar circulatory disease or symptom-complex which affects the extremities and which is marked especially by exaggerated sensitiveness of the skin. This hyperesthesia is such that any touch excites a sort of pain which the patient very much dreads. There often is but need not be spontaneous pain. Nevertheless it is so difficult to carry on everyday affairs without some contact of the part that in many a case the patient is made uncontrollably nervous, depressed and apprehensive. There are serious cases and mild ones, and it is the serious ones which have made the mild ones understandable.

Many years ago, S. Weir Mitchell[1] described the bad sort as causalgia, that is, burning pain. Those of you to whom this term means anything at all will recall that the word referred to a state of glossy redness of a hand or foot, atrophied soft parts, tapered digits, and nails much curved transversely. The burning pain, always present, was comparatively bearable until a touch or even a sound, a draft or a jar caused an agonizing increase. The patients, who were always wounded soldiers, soon became invalids, carrying about a bottle of water and a sponge with which they kept the limb moist at all times.

Mitchell's cases all resulted from wounds received in the Civil War and very little attention was paid to his descriptions until the War of 1914-18 produced a new and abundant crop. As a rule, a large nerve had been injured, very often some part of the brachial plexus, though if one nerve alone were involved, it was usually the sciatic or median. However, as experiences multiplied, it seemed that actually no nerve need be wounded. An artery might be damaged, and as the early symptoms were studied, the cyanosis, the sweating, the paroxysmal nature of the pain, all gave the impression of a sympathetic disorder. At least they did so to René Leriche,[2, 3] the champion of the sympathetic system as a participator in pain of all sorts. Leriche suggested that arterial wounds were really at the bottom of causalgia and pointed out that the median and sciatic nerves, and of course the brachial plexus, whose injured nervous tissue had seemed at first the basis of the lesion, have an abundant arterial supply.

It is now well known that arteries are well furnished with sensitory filaments, and it has been established (Moore[4]) that these filaments travel into the spinal cord with the posterior, or sensory, roots. How such fibers make reflex arcs with outgoing vasomotor nerves, the classical sympathetic system is, for the moment, unimportant. There probably are reflexes traveling by way of the spinal cord and there may even be local reflexes through plexuses upon the walls of the larger vessels. In any case, signs of sympathetic irritation, that is, sweating and peripheral vascular spasm, can be brought on by central-going impulses originating in and about the walls of the arteries and, for that matter, the veins. This is not the place to discuss the problem of why some of these reflex sympathetic disorders are painful and others not; why some leave the skin hot and others cold; why some are attended by edema and others by bone atrophy; why some appear to represent, in addition to everything else, paralyses of great mixed nerves. All are dysfunctions, into which the sympathetic system, primarily a vasomotor mechanism, enters in a very mysterious manner. How, for instance, is it related to pain? Clinical and physiological observations must in time give answer. At least it is fortunate that the causalgia-like states can be relieved, or at least improved, by a procaine block of the sympathetic supply to the limb in question, and that the relief lasts for at least the duration of the block. A clear case of pain and hypersensitiveness due to pure arterial irritation is the following:

A middle-aged man had suffered an arterial embolism. The embolus had become fixed in the left radial artery, which felt like a pencil, and could be followed without pulsation into the anatomical snuffbox. The hand was cool, a little pale, cyanotic and agonizingly sensitive to the touch. Two of the fingers, held partly flexed, were especially blue, cold and so very tender that the man guarded them at all times and refused to allow them to be straightened. When the plugged radial artery was resected under procaine, a sudden and dramatic change occurred. The hand not only *felt* comfortable to the patient but could now be freely handled. The color of the fingers at once improved.

Thus, fingers which were tributary to no outgoing nerves which could possibly have been influenced by the arterial resection were relieved of a painful vasospasm by the interruption of impulses travel-

*The Presidential Address delivered at the annual meeting of the New England Surgical Society, Salem, Massachusetts, September 29, 1939.

ing centrally along an artery. The accompanying anatomical diagram (Fig. 1) explains this contention.

One more bit of explanation. If a blood vessel is bruised or shocked by a bullet without suffering an actual wound, it goes into a state of spasm and

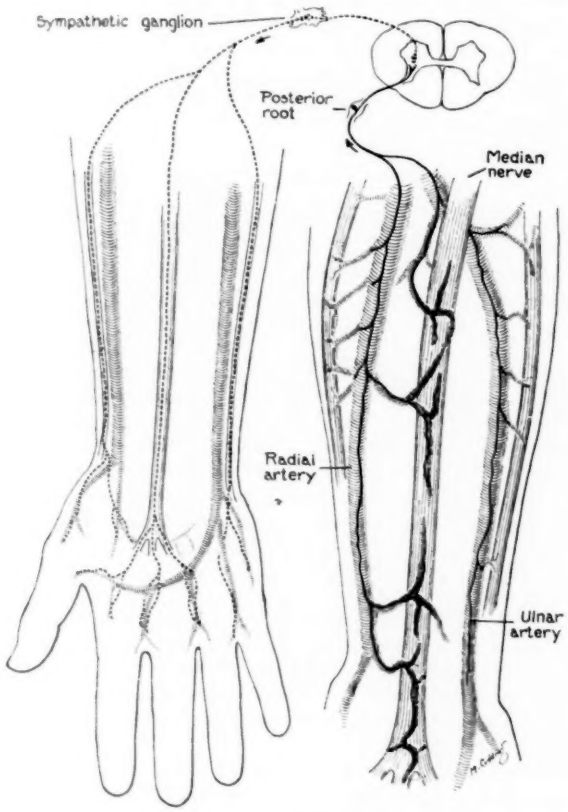

FIGURE 1. *A Diagram Representing a Possible Course of the Reflex Impulses Responsible for Causalgia, Traumatic Edema, Reflex Dystrophy and So Forth.*

In the limb on the right, the size of the median nerve and of the radial and ulnar arteries is exaggerated; the sensory (?) nerves of the arteries are shown in solid black lines, and the relation of these nerves to the small arteries of the median nerve can be seen (no attempt is made to show the arterial supply with its attendant nerves for the radial and ulnar nerves).

The nerves pass centrally along the arteries, enter the spinal cord in the posterior roots, connecting with outgoing sympathetic fibers. The supposed course of the reflex is indicated by arrows.

The sympathetic fibers are distributed via the great mixed nerves to the periphery, supplying the vessels of the hand in definite anatomical fields identical with the sensory distribution.

the tissues peripheral to the point of contact become pale, cyanotic and numb, perhaps absolutely insensitive. This is an acute, direct and probably local arterial spasm. Moreover it is often temporary. But if a blood vessel is irritated by pressure, or by minor infection; if the tiny nerves about a good-sized artery are teased, or if this teasing is extended to a multitude of small vessels in a limb, there may arise one of these strange, hyperesthetic, atrophic, sometimes edematous states which I am to describe to you. I will quote you one more case to illustrate the effect of a lesion affecting apparently the smaller blood vessels. This is taken from a publication of Lehman.[5]

D. E. D., a schoolgirl of 18, had suffered, 4 months before coming under observation, a punctured wound by a crabapple thorn upon the ulnar border of the right forearm. This had become infected and had been subjected to exploration and drainage. A sinus had been left surrounded by induration, heat and redness which extended halfway to both wrist and elbow. The patient feared to have the forearm touched and could barely move the wrist and fingers. During the following 7 months, four operations for drainage were performed. Almost a year after the original injury, the forearm and upper arm were swollen and doughy up to the axilla. Pain was increasing. The fingers were cool. The right radial and brachial arteries pulsated (to the touch) less strongly than those of the left hand. Though one of the old incisions was unhealed, the temperature and leukocyte count were normal. Amputation had been suggested.

On the ground that the condition resembled the "trophic edema" of some war wounds, and because tissue removed at the last operation had shown a perivascular inflammation, a periarterial sympathectomy was performed upon the right brachial artery. Two days after the operation, the fingers were a little less stiff and tenderness of the forearm had diminished. Six weeks later, motion at the elbow was free and that of the fingers was continuing to improve. Swelling had disappeared and the skin had become warm and dry. The wound had healed. In 6 months, except for some weakness, the extremity was normal. The disease had been cured by interrupting what seem to be ingoing arterial nerves.

That there is something basically at fault about the nervous systems of certain of the individuals affected, is probable. Some are insurance problems. Others have grudges against the world, or are perhaps stupid, or even criminal. It is easy enough to find fault with anyone who suffers from a disorder which seems to have no reasonable origin. For all of the ailments which touch off the causalgia-like reflex are commonplace and ordinarily are recovered from in a commonplace way. The reason that the strange states they occasion are not more often recognized is because of our extraordinary, indeed, infernal obstinacy in trying to fit things into categories. We think and teach that we can catalogue every diseased state we see. If we cannot catalogue it, we say it is not a diseased state at all. I suppose that in my everyday clinical experience, I am unable to explain at least thirty per cent of the patients' complaints. In this thirty per cent are included states which others doubtless understand and which would be clear to me if someone would lead me by the nose. I judge that in this "thirty per cent"

of many of you are included the reflex sympathetic disorders which are the subject of these remarks.

In recounting underlying causes I could begin with fractures, or thrombophlebitis or minor burns, but actually I will begin with a dog-bite.

M. F. D., a single woman of 37, was bitten on the back of the right hand by a dog. A local cellulitis rapidly developed. She entered the hospital 24 hours later. Her axillary lymph nodes were enlarged and her fingers stiff. She left the hospital in 3 days and soon seemed to have fully recovered; but 4 months later she returned. A few days earlier, the back of the right hand and thenar space had swollen. The fingers were a little bluish. They were held straight, the thumb adducted as in a median paralysis, the typical causalgia position. There was a brownish discoloration about the wound, which discharged a little serum. The x-ray showed some decalcifications of the bones and narrowing of the joint spaces. There was an intense hyperesthesia of both hand, fingers and forearm, yet light touch was poorly felt in the area of excessive sensitiveness to scratching or gentle pinprick. The patient was treated by hot soaks, the hand and forearm kept in a sling.

FIGURE 2. *M. F. D. An Instance of Mild Causalgia Following a Dog-Bite.*

Notice the smoothness of the skin of the right hand as compared with that of the left, especially the lack of transverse wrinkles over the interphalangeal joints. This photograph was taken five months after the bite was received.

Two months later, that is, 5 months after the original injury, the patient was still unable, because of hyperesthesia, to use her hand. Actually, she was considerably improved. There was a little brownish discoloration about the bites. The skin of the hand and fingers was smooth, as is shown in the photograph (Fig. 2). It was a little warmer to the touch than the other hand. At this time, a sympathetic block of the stellate ganglion completely removed, for the moment, all the sensitiveness to touch, pinching and pinprick. A rise of temperature to over 90°F. showed that a full sympathetic paralysis had been secured. The hand felt dry and hot. From this time on, improvement was steady and in a week or two the woman was at work again.

Here, then, is a mild causalgia, due to a (streptococcal?) infection following a dog-bite, and showing the typical smooth, hypersensitive skin, partial muscular paralysis and bone atrophy. There is a tendency to spontaneous recovery which the sympathetic block seems to have hastened.

The next is a case of a very different sort. At first sight, it seems hardly possible that it is related to the type of causalgia first illustrated.

J. D. T., a man of 30 years of age, about 2 years before was said to have strained his back lifting and was then discovered to have an inguinal hernia, which was believed to have been caused by the strain. Actually, his discomforts were probably due to a fractured lumbar transverse process which was only discovered later. However, an operation for hernia was performed and was followed by a right-sided femoroiliac thrombophlebitis. The thrombophlebitis left behind a leg which gave him an extraordinary amount of trouble. The lower part was slightly swollen and cyanotic, but the chief complaint was of hyperesthesia and pain. He not only suffered spontaneous cramps in the early morning but from a heavy numb feeling on walking. The purple color underwent a disagreeable red reaction on exposure to the sun. Subjectively, the foot felt cold.

Examination showed a diminished arterial oscillation in the right calf, equal posterior tibial arteries and a diminished right dorsalis pedis pulsation. Brisk walking brought on the numbness and increased the coldness of the right leg. The hyperesthesia was especially bad on squeezing the calf, as with a blood-pressure cuff. It included his whole leg, extending up to the right flank and back, the region of his fractured transverse process. It even spilled over into the left side of the back. The patient was unhappy, apprehensive and demoralized.

A right lumbar sympathetic block gave a typical rise of surface temperature for the right foot and relieved most of the hypersensitiveness. For perhaps 48 hours, the cramps and hyperesthesia disappeared, but at the end of this time both troubles recurred.

In this case, it is clear that the irritating lesion is perivascular, that is, about the great vessels in the region of the groin and pelvis, the scene of the thrombophlebitis. Leriche would advise, I think, separating the artery and vein (dividing the vein?) and a lumbar sympathectomy; and doubtless a very considerable procedure may be necessary to interrupt the vicious impulses. I have seen a somewhat similar result follow an axillary thrombosis.

In the two following cases, the causalgia is supposedly due to nerve injury. The first is of median

origin; the second is presumably due to division of the small sensory nerves upon the two sides of the outer phalanx of the thumb.

E. A. D., a married woman of 50 or so, had long haunted the outpatient department, complaining chiefly of arthritis. Recently, she had suffered a Colles's fracture of the left radius with marked posterior displacement. Reduction secured fair position and the hand was immobilized in acute flexion. Whether it was the initial injury or the flexed position which brought on the subsequent difficulties is not clear; supposedly the acute flexion, especially since it has been shown that in this position the median nerve is apt to be compressed between the hard edge of the transverse carpal ligament and the lower edge of the radius. However that may be, the fingers rapidly swelled, pain was severe and the palmar aspect of the wrist became blistered. A neutral position was at once adopted, but at the end of 6 weeks little motion had returned to the fingers and wrist. The hand was painful and edematous. Hyperesthesia of the hand and wrist was extraordinarily severe. The forefinger could not even be touched.

A procaine block of the sympathetic supply to the arm completely relieved all pain and sensitiveness, restoring much freedom of motion. The relief was, of course, only temporary, but from this time on the patient began to improve. She has since had her ups and downs, but all that is left is a somewhat numb, prickly feeling in the tip of the forefinger and thumb. That is to say, the causalgia is gone. The aftermath of a partial median nerve paralysis remains.

The last case to be quoted is that of C. O., a married woman, 30 years of age, who had been operated upon, 4 months earlier, for a felon of the right thumb. A "fish-mouth" incision had been made and had healed promptly, but increasing pain and tenderness, confined to the terminal phalanx, had then set in, so that even the lightest touch had become agonizing. The patient was unwilling to move the thumb and guarded it at all times.

An upper thoracic sympathetic block brought about a characteristic rise of temperature, that is, complete paralysis of all sympathetic impulses, and during the sympathetic paralysis, hypersensitiveness was dramatically relieved. The outer phalanx of the thumb could be handled and moved freely, but it was noted that between the incision and the nail, at the tip of the thumb, the skin was unpleasantly numb, as in the case of a skin field imperfectly supplied with sensation. During the day of injection, the hyperesthesia gradually returned.

It was held that a periarterial sympathectomy performed upon the radial artery at the wrist, by interrupting ingoing impulses traversing the vessel, would probably be curative. Accordingly, the veins associated with the radial artery, the loose tissues about the artery and the adventitia itself were removed for a distance of perhaps 5 cm. The result was as striking as was that of the sympathetic block. All hyperesthesia disappeared, leaving behind the unpleasantly numb area under the edge of the nail. Six weeks later, the comfort persisted though the patient still spared the thumb. The relief should be permanent.

You will appreciate, I am sure, how hard it is to see just what goes wrong in such cases, and you will feel this all the more when I tell you that other, somewhat similar results have followed a slight burn of the arm in an epileptic girl, an operation for Dupuytren's contracture of the hand, a cat-bite, the falling of an arm over the edge of the operating table or bed and the dropping of a block of wood upon the instep. Obviously, the sign which is most definitely common to all these cases is the hyperesthesia. That this is related to a sympathetic dysfunction is suggested by the remarkable effect of a sympathetic block upon the limb involved. However, this merely supports Leriche's contention that the sympathetic is concerned in some way with all pain. It does not tell how an infected dog-bite of the back of the hand causes the reflex irritation. It is perhaps safest to believe, for the moment, that perivascular sensitive fibers, whether lying upon a large vessel or surrounding many tiny arteries, whether in the soft parts or in the midst of a great nerve, are able to excite a prolonged, vicious, reflex, sympathetic disorder. The path of this reflex is not evident, but since it can usually, perhaps always, be broken by blocking or dividing the sympathetic gangliated chain, it may well pass into and out of the spinal cord. It can also be interrupted, as has been told above, along the course of the principal artery of the limb — the radial or the brachial, for instance, in the case of a causalgia originating in the hand. It is not easy to reconcile this reflex mechanism, which seems to use a sympathetic pathway, with Sir Thomas Lewis's[6] recent observations upon pain and sensitiveness of the parts about an injury. As a result of experiments upon human beings, he finds that pain, tenderness and the vascular flare are related to hitherto unrecognized "nocifensor" nerves, that is, nerves having a function different from the sensory fibers of the skin. He believes that the stimulation of injury excites these widely arborizing neurons, through axon reflexes, to activate in some way the sensory nerves, lowering their threshold to pain. At the same time, the nocifensor reaction calls forth a vascular dilatation. Yet its neurons are not a part of the sympathetic system and act in its absence, having their cell bodies in the sensory, posterior-root ganglia. Lewis finds further that these same nocifensor fibers can be irritated to action by injury to a large nerve trunk, so that they may well be responsible for causalgia and causalgia-like states. Certainly the mechanism he describes is admirably adapted to setting up and maintaining this peculiar symptom-complex. Unfortunately, it still leaves much to the imagination, ignoring the obvious relief offered by sympathetic block, whether temporary or permanent. Doubtless, many more painstaking anatomicophysiological researches must still be undertaken.

Whatever their origin, the minor causalgias

which I have described are a cause of much misery. Recently, Livingston[7] has very fully discussed them. He is particularly interested in discovering the spot from which the reflex seems to have arisen, the point of injury. Indeed, his paper is entitled "Post-Traumatic Pain Syndromes" and he has demonstrated that the injection of procaine into the "trigger point," repeatedly if necessary, may be curative. My own tendency has been to attempt interruption of the reflex arc, at *any* available point, by procaine block or surgical excision. You will notice, however, that most cases do not come to surgery. The disorder is often functional, not at first, perhaps, but later. It is overlain by hysterical symptoms. It is subject to the "compensation neurosis" so familiar to the insurance companies and their physicians. If you think that for such reasons this is a dangerous field for all who are not thoroughly familiar with it, at least you will agree that it is a fascinating field; and you will realize that the cure of patients suffering from a causalgia-like state is likely to earn their whole-hearted gratitude. The painstaking study of common ailments is just as full of rewards as it ever was, and the causalgias are rather common in medical and surgical practice today. They certainly fall among the thirty per cent of cases as to which most of us are blind or ignorant. I suggest that you keep them in mind.

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EXTREME LEUKOCYTOSIS AND ACUTE HEMOLYTIC ANEMIA ASSOCIATED WITH THE ADMINISTRATION OF SULFANILAMIDE*

Report of a Case

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IN VIEW of the seriousness of the acute hemolytic anemias that occasionally follow the administration of sulfanilamide, the following case seems worthy of record.

CASE REPORT

C. C., a 34-year-old Negro porter, was admitted to the Parkland Hospital on July 29, 1939, complaining of a swelling in the perineum and marked weakness. Several weeks previously, he had developed a urethral discharge, followed by difficulty in urinating. An abscess had appeared in the perineum, which was incised and drained by his local physician 5 weeks before entry. He was given a few "white tablets" at this time, of an indeterminate nature, with no noteworthy effect. Four days before entry, in the Outpatient Department, the perineal abscess had been reopened and the patient started on sulfanilamide. At home, he gradually became weaker and stuporous, and was admitted to the hospital. At the time of the first blood examination he had taken eighty-four 5-grain tablets of sulfanilamide, making a total of 420 gr. over a period of 5 days. He had had gonorrhea 14 and 11 years previously, cured by local treatment. Fourteen years before entry he had had a chancre, and had taken antisyphilitic treatment for a year at that time.

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The temperature was 101.6°F., the pulse 120 and the respirations 22. The patient was well developed, lethargic and obviously acutely ill. The mucous membranes were extremely pale. The tongue was coated and pale. The lungs were normal. The heart rate was rapid, with a loud systolic murmur at the apex. The blood pressure was 116/52. Examination of the abdomen showed a fluctuant, tender, reddened, subcutaneous mass in the suprapubic region pointing in the midline 5 cm. above the symphysis. The skin of the penis was undermined by a dissecting abscess. The entire perineum was tense and bulging, with several sinuses draining foul, purulent material. The scrotum was markedly edematous. Rectal examination was essentially normal. There was no lymphadenopathy.

Examination of the blood revealed the following: Red blood cells 1,240,000; hemoglobin 21 per cent (Sahli); white blood cells 140,000, of which 36 per cent were segmented polymorphonuclears, 13 per cent juvenile neutrophils, 18 per cent band forms, 22 per cent lymphocytes, 2 per cent monocytes, 6 per cent myelocytes and 3 per cent myeloblasts. The smear showed achromia, poikilocytosis and polychromatophilia. An average of 5 normoblasts was seen in counting 100 leukocytes. Urinalysis showed a cloudy, amber specimen with a specific gravity of 1.010, a ++ albumin test and no sugar. The sediment contained 18 to 20 leukocytes per high-power field, a moderate number of erythrocytes and a few granular casts. The urinary findings were considered due to the local infection. Kline, Kahn and Wassermann reactions were positive.

Subsequent laboratory data are shown in Table 1. The

elevated blood-nitrogen level was interpreted as being caused by the urinary tract obstruction.

Diagnoses of periurethral abscess, with extension, and acute hemolytic anemia associated with the administration of sulfanilamide were made. The high leukocyte count could not be explained, but the possibility of a leukemia as a cause of the whole picture was entertained. In any event, surgical drainage of the septic areas and blood transfusions seemed indicated.

On the day after admission, the patient was given a light nitrous oxide and oxygen anesthesia, and rapid, wide incision and drainage of the perineal, scrotal and suprapubic lesions were carried out. An external urethrotomy was also done, through a strictured membranous urethra. The patient was given 600 cc. of citrated blood and was returned to the ward in poor condition.

For 48 hours the patient appeared in critical condition. He was given frequent blood transfusions, intravenous glucose and constant inhalation of oxygen through the Boothby mask. On the 3rd postoperative day he showed definite improvement, and thereafter gradually recovered. The urethrotomy tube was removed at the end of a week, and the wounds granulated in rapidly. Sounds were passed during the convalescence. The patient was discharged on the 24th hospital day. He has been seen in the Outpatient Department, and continues in satisfactory condition.

Table 1. *Clinical Laboratory Findings.*

Hospital Day	Hemoglobin (Sahli)	Red-Cell Count	White-Cell Count	Blood Urea	Blood Creatinine	Icteric Index	Transfused Blood	Remarks
	%	$\times 10^6$	$\times 10^3$	mg. %	mg. %		cc.	
1	21	1.24	140	—	—	—	—	Myeloblasts and myelocytes in smear
2 (operation)	—	—	108	—	—	—	600	Myeloblasts and myelocytes in smear
3	—	—	—	93	2.3	16	500	Myeloblasts and myelocytes in smear
4	—	2.40	54	—	—	—	625	Reticulocyte count 52 per cent; 11 normoblasts and 6 myeloblasts seen while counting 100 leukocytes
5	—	2.70	19	47	1.5	10	600	
7	76	3.60	11	—	—	—	500	
10	80	3.80	10	36	1.7	6	—	
21	—	4.0	7	—	—	—	—	

The acute form of hemolytic anemia following sulfanilamide therapy is one of the most serious complications of this drug. It is to be distinguished from the comparatively slight, slowly developing drop in hemoglobin that commonly occurs when sulfanilamide administration is prolonged for ten days or more. Harvey and Janeway[1] first described the acute anemia associated with sulfanilamide, reporting 3 cases. Later, Wood[2] discussed the condition and reported on 21 cases of acute anemia occurring in 522 patients treated with sulfanilamide, an incidence of 4 per cent. That this figure is probably considerably higher than the average is indicated by the comparatively few reports in the literature and by the fact that at Parkland Hospital, where over 2000 patients have received the drug under adequate precautions, no case of acute hemolytic anemia, other than the one here reported, has been encountered.

The extremely high leukocyte count in our case in contradistinction to the granulocytopenia that is usually considered a hazard of sulfanilamide administration prompted us to analyze several cases of acute hemolytic anemia reported in detail in the literature.[3-7]

The acute anemia is usually ushered in early in the course of sulfanilamide therapy in a patient apparently responding satisfactorily to the medication. Nausea, dizziness, pallor, jaundice, malaise, weakness and fever are clinical manifestations, while the erythrocyte count and hemoglobin content of the blood fall rapidly and sharply. The signs of anemia may come on from thirty-six hours to seven days after beginning treatment, the average time of the maximum anemia being five days after onset of use of the drug. No case has developed after the first week of treatment. Cases have occurred in patients from ten months to sixty-four years of age. The conditions for which the drug was given have been varied, and there is no relation between the occurrence of the anemia and the type of infecting organism.

The process seems unrelated to the dosage of sulfanilamide or to its concentration in the blood. In a twenty-six-year-old woman, a severe anemia ensued thirty-six hours after the administrations of only 100 gr. The highest blood concentration of sulfanilamide found by Wood in his anemia cases was 10.7 mg. per 100 cc., whereas blood levels as high as 40 mg. were observed in patients not developing anemia.

The pathogenesis of the disease is not well understood. That the anemia is due to a rapid peripheral hemolysis is shown by the sudden drop in the hemoglobin and red-cell count, the rise in the icteric index, the presence of excessive amounts of bile pigment in the urine and, occasionally, frank hemoglobinuria. There is no increase in the fragility of the erythrocytes. In the 2 fatal cases reported, necropsy has revealed erythropoietic hyperplasia in the bone marrow, which is the usual response to peripheral blood destruction, and there has been no sign of bone-marrow depression such

as occurs in the aplastic anemia following arsenic or benzol poisoning.

Harvey and Janeway point out the similarity of this type of anemia to the hemolytic crises produced by phenylhydrazine, and suggest that susceptible individuals may produce a toxic product from the sulfanilamide having a phenylhydrazine-like action. Wood found that in 4 of 5 patients in whom the drug was repeated after the development of an acute hemolytic anemia during their first course, a recurrence took place. All the evidence would thus seem to warrant classifying this disorder as one of drug idiosyncrasy.

TABLE 2. *Comparative Blood Findings from the Literature.**

SOURCE	HEMOGLOBIN %	RED-CELL COUNT $\times 10^6$	WHITE-CELL COUNT $\times 10^3$
Harvey and Janeway[1]			
Case 1	30	1.57	87
Case 2	18	2.0	30
Case 3	40	2.02	32
Kohn[3]	40 (6.0 gm.)	2.0	47
Wood[4]	22 (3.5 gm.)	1.13	26
Koletsky[5]	45	1.45	24
Antopol, Applebaum and Goldman[6]			
Case 1	25	1.5	56
Case 2	50	2.2	21
Spence and Roberts	21	1.24	140

*In 7 of the cases myeloblasts, myelocytes and nucleated red-blood cells were noted.

The leukemoid blood picture in our case seems an exaggeration of the moderate to marked leukocytosis in other reported cases (Table 2). We have no explanation of its mechanism beyond suggesting that it may have been simply a concomitant of the marked bone-marrow stimulation and hyperplasia. A leukemoid reaction with sulfapyridine has recently been described by Moody and Knouf.[8] Some idea of the marrow activity is shown by the occurrence of 52 per cent reticulocytes on one occasion in our case.

The treatment of the acute anemia involves withdrawal of the drug, forcing of fluids and maximum transfusions of blood. The convalescence is strikingly rapid after the patient surmounts the hemolytic crisis. In one of the 2 reported deaths, no blood was available for transfusion, and in the other, the amount of blood given was apparently inadequate.

SUMMARY

The acute form of hemolytic anemia following sulfanilamide therapy is characterized by a rapid fall in the erythrocyte count and hemoglobin content of the blood during the first few days of sulfanilamide administration. The process is apparently a peripheral hemolysis due to an idiosyncrasy to the drug and is unrelated to the dosage, concentration of sulfanilamide in the blood or type of infection. The bone marrow shows evidence of hyperplasia.

An accompanying moderate to marked leukocytosis has been noted as a part of the syndrome, but has not been emphasized. The case reported illustrates the occurrence of a leukemoid blood picture and the marked height to which the leukocyte count may rise in this condition.

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REPORT ON MEDICAL PROGRESS

ENDOCRINES: THE USE OF TESTOSTERONE*

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THE drug testosterone is worthy of lengthy discussion, for when its use is indicated it is powerful and of considerable value. Indeed, in my experience this is one of the most potent drugs recently introduced to medicine. Because its effects are so definite and widespread, its use should be regulated with careful judgment and understanding. Testosterone is a synthetic preparation apparently identical with the active hormone that has been isolated from the testes by Laqueur and his associates.[1] It is more potent than the androgen (male hormone), androsterone, which has been isolated from the urine. In preparing the drug, it is now generally made as testosterone esters, and the propionate is now commonly employed, for it produces a more prolonged effect than does the simpler testosterone. These drugs must be injected parenterally, though recently the use of an inunction has been introduced. Intramuscular doses are large and are commonly 10 to 25 mg. of the crystallized synthetic compound, injected as often as three times a week. While this is a large amount in endocrine therapy, it has at least a counterpart in the excretion rates. In normal individuals, both male and female, the ratio of urinary excretion of androgens to estrogens lies between 500:1 and 1000:1 in terms of weight; so it is not surprising that similar ratio differences are found in the amounts necessary for therapeutic purposes.

It has long been well known that androgens are excreted in the urine of both males and females, and in fact in fairly high concentration. Recently, Nathanson, Towne and Aub[2] have studied excretion in children, and have found that even children of three years of age have a definite androgen excretion which gradually increases as puberty approaches. Boys, as well as men, have a higher output than have females. However, there is no cyclic excretion of androgens as there is of estrogens, and therefore it is not necessary to do repeated observations in the study of the androgen excretion if this determination appears necessary before instituting therapy.

It must be remembered that though the effects of testosterone esters are apt to be striking, their use is a pure substitution therapy, just as is that of insulin. Testosterone does not stimulate the pituitary gland to greater activity; in large doses, indeed, it appears to inhibit temporarily this important gland. The result is that testosterone does not stimulate the growth of the testes. It substitutes for the active secretion of that gland, and does this only so long as its injection is continued. McCullagh[3] has reported, and Nathanson's work[4] confirms, that when testosterone is injected the androgens rise abruptly in the urine but return to their original level within forty-eight hours after the injection. But not all injected testosterone appears in the urine. What becomes of the remainder is not known. If a large dose of testosterone is given to individuals who are already excreting androgens, after forty-eight hours the excretion level falls below the original level, suggesting an inhibiting effect on the sex-stimulating hormone of the pituitary gland.

When testosterone is injected into women, the undesirable sequelae of hypertrichosis, enlargement of the clitoris and deepening of the voice may occur. The hypertrichosis may last for some months, and has been said to remain even longer in old people. While these results have usually come only with the use of very large amounts of the drug, such changes have been observed with therapeutic doses. This possibility must be constantly borne in mind when the drug is employed in women. These undesirable effects of testosterone are described by Greenhill and Freed[5] in 2 women who received 50 mg. every two or three days. They soon complained of increasing hair growth, and in one of them this was still present four months after the last injection. While this must be taken as a warning in regard to the use of testosterone, the amounts they received are probably larger than necessary for therapeutic effects.

Testosterone and its esters appear in my experience to be well tolerated, though their effects on the general feeling of patients may vary. Frequently patients respond with an increase of general vigor, though I have seen occasional responses of fatigue and lassitude. It is nearly impossible to dissociate these reactions from purely psychologic responses to injections, but objective

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evidences of the action of testosterone are obvious in many clinical conditions. The literature on this subject is rapidly enlarging, and though the following report is not based on a complete bibliography, it covers most of the important recent articles on the subject.

The Council on Pharmacy and Chemistry[6] of the American Medical Association recently issued a most interesting and instructive report on the present status of testosterone, and decided not to include these preparations in its book *New and Non-Official Remedies* until the preparations had been properly evaluated by ample clinical experience. This decision was arrived at because of the varied claims made for the new drugs. It is obvious that a compound such as this needs careful evaluation before it can be recommended, and much exploratory work needs to be done before its applications in medicine will be well understood.

Use for Hypogonadism in Males

The best treatment for hypogonadism would be to stimulate the anterior pituitary gland to greater activity, and so indirectly stimulate the gonads. But a good technic for so stimulating the pituitary gland is not at hand. Thyroid medication does this to a moderate degree, but its effects are not dramatic. Substitution therapy for diminished anterior-pituitary activity, in the form of gonadotropic hormones, of anterior-pituitary-like hormone or of pregnant mare's serum concentrate, may have the effect of stimulating the growth of the testes temporarily, but it does not have the slow, prolonged influence of the pituitary gland itself. The anterior pituitary gland obviously has a very slow action. Nathanson, Towne and Aub[2] have shown its influence on androgen excretion as early as five years of age, with a gradual crescendo up to puberty. The gland therefore appears to have a prolonged stimulating effect, and similar sluggishness of effects should be expected from the physiological doses of substitution therapy. Of course, if larger doses are used, more rapid results are to be expected, though, like most effects of anterior-pituitary therapy, the active response may be of only a few weeks' duration.

The injection of testosterone or its esters has a more rapid effect, for this appears to be the activating hormone for the male secondary sex characteristics. Though it produces some of these effects in a period of weeks, it has no clear-cut stimulating effect on the testes themselves. There is, indeed, some evidence of a reverse effect, as judged by spermatozoa counts.

Hypogonadism in males demonstrates the most obvious effects of testosterone. McCullagh[3] recently published an excellent paper on the results of testosterone therapy in 6 cases of testicular deficiency at puberty. He showed that before treatment these patients excreted very little androgen in the urine, and that injected testosterone was promptly excreted, mostly within twenty-four hours. In cases of severe prepuberal hypogonadism he found that testosterone injections produced stimulation of all secondary sex characteristics in males, though prostate enlargement was the last to develop. The testicles did not seem to enlarge, but the number of spermatozoa did not decrease. The closing of bone epiphyses was not accelerated by testosterone — an observation of considerable significance in growing children.

McCullagh obtained good results in adult functional hypogonadism. In the adults treated by Nathanson and Aub,[7] the results are equally striking. Erections and enlargement of the penis rapidly occur, followed by the growth of hair, changing of the voice and a moderate change in body configuration. The prostate enlarges to normal size as judged by palpation, whereas before treatment the gland could not be felt. Greater psychologic vigor and assurance are obvious, though these may well be purely psychologic responses to the physical changes.

Dunn[8] confirms the stimulating effects on secondary sex characteristics, and also lays stress on the psychologic effects. He describes an improved mental concentration and interest in social activities, as well as improved physical energy and endurance.

The reports of Webster[9] and of Eidelsberg and Ornstein[10] are similar. The latter have administered testosterone for many months in the usual doses of 50 to 75 mg. per week. They have not observed a diminution in effect as the months go by, either in body changes or in an improved feeling of well-being and increased strength. Kearns[11] agrees as to the value of the drug when given intramuscularly, but also shows that it can be administered as an inunction in a greaseless base. With the daily careful rubbing in of such an ointment, containing 4 mg., he obtained as satisfactory results as with injections. As proof of its absorption, he found increased androgen excretion in the urine.

All these dramatic effects appear to continue so long as testosterone therapy is maintained, and vary directly with the amount given. When therapy is stopped the eunuch returns in a period of weeks to his original state, though the deepened voice appears to be maintained.

It is to be expected that testosterone would be tried in many other conditions. Zehn[12] believes that daily 10-mg. injections of testosterone

constitute excellent treatment for benign hypertrophy of the prostate. This has also been reported by others, but not enough information has accumulated in regard to this difficult subject to warrant a conclusion as to its value.

Uses in Females

Large doses of testosterone, like estrogens, apparently inhibit the production of sex-stimulating hormones by the pituitary gland so that uterine bleeding is inhibited. This results in an unstimulated ovary and hence a lack of secretion of ovarian hormones. Testosterone does not appear to have a depressing effect on the uterus itself,[13] in fact it exerts some stimulation directly even in ovariectomized females.[14]

The excellent result of the injection of testosterone at the menopause is a puzzling phenomenon, inasmuch as one would expect estrogens to be the drug indicated at that time. However, the work of Nathanson and Towne[4] shows that in castrated women only a small quantity of injected testosterone is excreted in the urine as androgens. There is, on the contrary, a discernible increase in the total urinary estrogen output, and also a depressing effect on the pituitary gland, as evidenced by a decrease in the urinary follicle-stimulating hormone. From its excretion products one must suspect that it is changed in part to estrogens. If one uses small, single doses, however, one may get other effects, as shown by Nathanson, Franseen and Sweeney[15] in immature female rats. By the injection of a single dose of testosterone propionate there resulted a direct effect on the vagina, which produced a premature opening and an estrous response, as well as a direct effect on the uterus, and indeed an indirect stimulating effect on the ovary through stimulation of the anterior pituitary gland. It is the depressing effect on the pituitary gland of repeated doses that may account for the satisfactory effects it produces in the annoying symptoms of the menopause.

There is some evidence that testosterone also has an inhibiting effect on the peripheral female hormones, the estrogens. Thus Lipschütz[16] has produced evidence that large doses of testosterone will inhibit the effect of Estradiol in castrated female guinea pigs, an effect characterized by an increase of weight, of musculature and of fibroids of the uterus. The use of testosterone propionate in the treatment of so-called "essential" dysmenorrhea, therefore, has some basis according to physiological knowledge. This type of pain, produced by contractions of the uterine musculature, seems relieved by the corpus-luteum hormone and intensified by estrone. Since testosterone appears antagonistic in some ways to estrone, there would seem to be some justification for its use in this syndrome. Rubinstein and Abarbanel[17] found that it relieved most cases of essential, though it was not so helpful in anatomically determined, dysmenorrhea. Salmon, Geist and Walter[18] also treated patients in this way. In 26 of 30 cases they obtained satisfactory results, and two thirds of the 25 cases followed for more than three months remained symptom-free. If 500 mg. of testosterone propionate was given there was danger of hirsutism and change in voice; but the necessary dose is below this amount, and they recommend 250 to 350 mg., to be given during one cycle. They advance the theory that functional dysmenorrhea may be caused by an androgen deficiency.

Geist, Salmon and Gaines[19] gave intramuscular injections of testosterone (300 to 1000 mg. a month) for menorrhagia to patients who showed no gross evidence of disease. Bleeding stopped in 18 out of 20 cases, and uterine biopsies showed that this was usually accompanied by disappearance of the secretory phase, or even inhibition of the proliferative phase of the uterine endometrium. Menstruation, therefore, ceased, but within a month after stopping treatment the ovarian effects on the uterine mucosa again became evident and regular bleeding usually became re-established. These effects are again suggestive of the temporary inhibitory effect of testosterone on the sex-stimulating hormones of the pituitary gland.

To 38 women with functional uterine bleeding, Mazer and Mazer[20] gave intramuscular injections of testosterone three times a week for from two to nine weeks. The total dosage per month ranged from 30 to 300 mg. A cure was considered to have occurred if the abnormal bleeding ceased and did not recur for at least four months after the discontinuance of treatment. By these criteria 68 per cent of the women were cured. It is interesting to note that the menstrual rhythm in the 30 patients who were menstruating regularly before the onset of the abnormal uterine bleeding was not disturbed.

Miscellaneous Uses

It would be natural to expect that testosterone with its suggestive antagonistic effects toward the estrogens would be effective in counteracting abnormal development of the breasts,[21] and this should be particularly true in abnormal growth of the male breast. Hoffman[22] tried such treatment in 28 males and found regression in 12 cases and a reduction of more than 75 per cent in 9 others, while in 2 cases there was complete failure. However, spontaneous regression occurred

in 3 untreated cases. Wernicke[23] also tried this therapy in 4 cases; he obtained good results in 2, inasmuch as the gynecomastia disappeared, but there was a spontaneous recurrence in 1 case after therapy was stopped. On the other hand, Turner[24] did not find that testosterone influenced this condition in a man who had otherwise normal secondary sex development. It is important to remember that this disease improves spontaneously, and too much stress should not be laid, therefore, on improvement in a few cases. A larger amount of data is necessary before conclusions can be reached.

A more definite influence of testosterone on lactating breasts is indicated in a paper by Kurzrok and O'Connell,[25] who treated 21 consecutive cases through early puerperiums in which lactation was considered undesirable. The patients were given repeated injections of testosterone propionate intramuscularly, usually in 25-mg. doses twice a day until a total of 50 to 150 mg. had been given. Only 2 of these 21 cases appeared to be treated unsuccessfully, and the symptoms associated with inhibition of lactation were relieved within twenty-four hours without the addition of any other therapeutic measures. As soon as complete relief of symptoms was obtained hormone injections were stopped, and no unpleasant aftereffects were observed.

This work has been confirmed by Beilly and Solomon,[26] who treated 108 consecutive postpartum cases with testosterone propionate. They obtained optimal results in 58 per cent and a lessening of milk production in 40 per cent, and the effectiveness did not seem to be related to the postpartum date of beginning treatment. They also found no deleterious effects from therapy, and no obvious breast-tissue changes were observed.

The use of testosterone propionate in the treatment of chronic mastitis was described by Spence.[27] He reports a relief of pain in 14 of 16 cases, and a reduction of the nodules in the breasts of two thirds of his patients. He used quite large doses of the drug and described, unfortunately, increased hirsutism in several young patients.

That testosterone will improve eczemas and psoriasis in women with menstrual disorders and in some men is asserted by Lafitte and Huret.[28]

Arndt[29] claims that testosterone will give a prolonged improvement in patients with neurasthenia and in men suffering from intermittent claudication, even with early gangrene, and from angina pectoris. That about twelve injections of testosterone greatly improved — and indeed cured — many of the severe psychoses associated with the menopause is claimed by Weiss.[30]

Summary

From this report of the practical use of testosterone in clinical medicine it is obvious that the drug is a potent one, particularly in hypogonadism in males. In this condition its effectiveness as substitution therapy is uniformly accepted. For other diseases for which it has been recommended more careful observation is essential before definite conclusions can be reached. The evidence for its effectiveness in prostatic hypertrophy varies. Its use in females is the more interesting development of the last year or two, and at the menopause it often seems to be even more effective in controlling vasomotor difficulties than are the estrogens. Its value in dysmenorrhea and abnormal bleeding is asserted, but needs further confirmation; and its help in drying up postpartum breast secretion has been confirmed with a reasonably large series of cases. It is therefore likely that in the next several years the use of testosterone for various abnormalities will become better established. This is not surprising, inasmuch as androgens are actively secreted, in both men and women, and probably purely by their antagonism to estrogens play an important role in hormonal control of the sex cycles. Of all the recent endocrine drugs, testosterone and its esters are at the moment the most interesting, as is well attested by the enormous number of publications appearing in regard to their use.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26211

PRESENTATION OF CASE

First Admission. A fifty-seven-year-old Swedish cook was admitted to the hospital complaining of indigestion of some ten years' duration.

For ten years the patient had experienced transient, recurrent, increasingly frequent attacks of indigestion, associated with cramp-like pain in the epigastrium and right upper quadrant of the abdomen, often radiating to the right hypochondrium and mid-back. These attacks were precipitated by the ingestion of greasy or fatty foods and were accompanied by nausea, vomiting and a feeling of epigastric fullness with flatus. No jaundice, constipation, diarrhea, chills, fever, clay-colored stools, or dark urine was noticed until the last episode, the morning of admission to the hospital, when she ate a breakfast consisting of an egg, toast, butter and coffee with cream. A few minutes later a typical, severe attack ensued. However, the upper and right abdominal pain failed to remit with the usual remedy, namely, baking soda. At noon that day she experienced a severe shaking chill, which lasted thirty minutes. Because of these complaints she was brought to the hospital for treatment. The past and family histories were noncontributory. The menopause had occurred five to six years before admission. She had had no hot flashes, but had had two menstrual periods since that time, the last occurring eighteen months before admission. A uterine suspension with appendectomy was performed in an outside hospital twenty years before admission.

Physical examination revealed an obese, slightly pale woman who complained of pain in the right upper abdominal quadrant, where there was also localized tenderness with slight muscle spasm. No abdominal or pelvic masses were palpated. The remainder of the physical examination was essentially normal.

The temperature was 101°F., the pulse 108, and the respirations 28.

Examination of the blood showed a red-cell count of 3,500,000 with a hemoglobin of 90 per cent (Tallqvist), and a white-cell count of 13,000 with 75 per cent polymorphonuclears. The urine was negative, no bile being present. Stools were soft, formed and dark brown. The blood Hinton test was negative. The van den Bergh test was 6.67 mg. per 100 cc., with a biphasic reaction.

The temperature, pulse and respirations fell to normal levels on the day after admission, and except for slight jaundice which appeared and soon vanished, the patient's symptoms improved steadily. She developed a mild upper-respiratory infection, and on the seventh hospital day, when the latter had subsided, a laparotomy was performed under general anesthesia. On exploration of the abdomen the tubes and ovaries were normal to palpation. The uterus was found to have been suspended at the previous operation, but had remained adherent only on the right side. Exploration of the cecum revealed that the appendix had been removed at the previous operation. There were a moderate number of adhesions about the gall bladder, but no very marked signs of inflammation. This organ was removed, and the common duct was explored and drained. Many pigmented stones of various sizes were found in the gall bladder and common bile duct.

The patient enjoyed an uneventful postoperative course, and was discharged on the thirteenth postoperative day.

Final Admission (six months later). Following discharge from the hospital, the patient improved steadily and satisfactorily, but never quite regained her normal vigor. Approximately two months before the second admission she began to experience, for the first time, dull, aching pains in the right lower abdomen. These came and went, lasted a few minutes to an hour or two and recurred irregularly one to four times a day for a week or more at a time. The discomfort caused her little distress as it was never so severe as the pains she had experienced before the cholecystectomy was performed. About one month before admission she began to notice attacks of "indigestion," characterized by ill-described but apparently severe pain in the epigastrium, which radiated around the torso to the right back and sometimes to the left hypochondrium. These episodes usually occurred in the midafternoon and again in the early morning hours, and became so frequent that they were a daily occurrence. Relief from the discomfort was obtained by massaging the abdomen until vomiting followed. The vomitus was usually sour, rarely bitter, and at no time contained evidence of fresh blood. She became anorexic, noted increasing fatigue and torpor, and complained of constipation and gas, which were relieved only by oil or cathartics. She had lost about 6 pounds during the month before reentry. She continued to work until two days before admission.

Physical examination showed a firm, tender, smooth, rounded mass, measuring about 10 cm. in diameter, in the right lower quadrant. It shifted with respiration and by palpation in a cephalad or caudad direction, and was definitely outlined by the examining hand.

The temperature, pulse and respirations were normal.

The blood showed a red-cell count of 4,340,000 with 13.6 gm. hemoglobin (photoelectric-cell technic), and a white-cell count of 7500 with 58 per cent polymorphonuclears. The urine was negative. The stools were brown, soft, formed and guaiac positive.

A barium enema passed to a point just above the cecum that corresponded to the upper border of the palpable abdominal mass. At this point a temporary delay was noted, and the barium was seen to pass suddenly into the cecum and ileum. A rounded mass was seen projecting upward into the ascending colon, and the ileum lay in the center of this mass. The ileum was slightly dilated, its margins were irregular, and there was complete absence of the mucosal markings. There also appeared to be destruction of the colonic markings around the ileocecal valve. The cecum was reduced to a small crescentic cavity lying along the lateral margin of the mass. After evacuation the appearance was much the same except that the upper margin of the mass projecting into the colon was better demonstrated. Filling the colon with air gave no additional information.

On the sixth hospital day, an operation was performed.

Differential Diagnosis

Dr. James E. Fish: The question immediately arises in a situation of this sort as to whether the secondary condition which brought about the re-entry co-existed at the time of the original entry, or whether it developed as a complication of the first condition or perhaps as a complication of the operation. A mass appearing in the abdomen a matter of months following an abdominal operation, of course, makes us think of the possibility, even though we do not believe it is likely, of a sponge that had been left in the abdomen. We can assume that the "sponge count" was correct. Furthermore, the sponges at the Massachusetts General Hospital have attached to them a metal clip; hence, a sponge in the abdomen would show immediately on x-ray examination with a flat plate. Furthermore, the mass described by x-ray does not suggest that sort of complication. So I think we can rule out any such possibility as a cause for this mass in the right lower quadrant.

In summary of this rather long history, I am inclined to believe the first episode was a clear-cut attack of choledocholithiasis. The fever and chill in the absence of more marked evidence of inflammation in the gall bladder are undoubtedly accounted for by some slight degree of liver involvement — a cholangitis. She had a severe chill on the first admission to the hospital, and a van den Bergh that might suggest liver damage. The finding at operation of small stones in the common duct as well as in the gall bladder is certainly in keeping with such an assumption. It therefore seems proper to discard the first operation as having any direct relation to this second episode. The first operation, therefore, becomes of interest to us only from the point of view of knowing whether the cecum was perfectly normal at the time of the abdominal exploration or whether some lesion was present but overlooked.

Let us run through some of the symptoms. We notice that the patient did very well for four months — another fact that certainly is against any complication from the operation. Then after four months she began, for the first time, to have dull aching pain in the right lower abdomen. This came and went. It is not described exactly as peristaltic pain, and yet it does suggest that type of pain. A little farther on we get additional information about the pain; namely, that it was severe in the epigastrium and that it radiated around to the back and sometimes to the left hypochondrium. The pain is not exactly typical of small-bowel pain but certainly is not inconsistent with it in the presence of partial or intermittent obstruction. I can attach no significance to the fact that the pain occurred in the midafternoon or early morning hours. There was a progressive factor in that the pain became more and more frequent until it was a daily occurrence. The patient obtained relief by massaging the abdomen. That is an extraordinary observation, if correct, and it would seem to fit into the ultimate picture. Whether she obtained relief by the vomiting that followed or whether she in some way displaced the tumor mass in the abdomen by massage is not clear. I cannot attach any particular significance to the type of vomitus. We now note the presence of constipation and gas. These additional symptoms plus nausea and vomiting are common symptoms of intestinal obstruction, even in a mild degree. She lost some weight, — 6 pounds during the month before admission, — and yet with all this partial intestinal obstruction the individual was well enough between episodes so that "she continued to work," confirming the impression that her difficulties were due to partial and intermittent obstruction.

On physical examination she had a fairly siza-

ble tumor — the size of a man's fist; it shifted with respiration and, still more important, it shifted in an up-and-down direction on palpation. Apparently it did not shift laterally very much. That would suggest that it was in the cecum, since the cecum, being tied down unlike the small intestine with its longer mesentery, might only move up and down in this manner. If it were a mass in the small intestine it would move more freely in all directions. Furthermore, the lack of more pronounced fixation would suggest that the tumor was not retroperitoneal. We note further that the temperature, pulse and respirations were normal and that the white count was fairly low. This is all very strong evidence against the presence of an inflammatory mass. The positive guaiac test is important, but not especially diagnostic. It suggests, certainly, an erosion or break in the lining of the mucous membrane, but we do note positive guaiac tests in the stools even with inflammatory processes outside the bowel wall. I even remember positive guaiac tests in several cases of appendiceal abscess. From the description of the barium enema we certainly get the impression that the mass surrounded the end of the ileum projecting into the bowel and that brings to my mind particularly the thought of an intussusception of the ileum into the cecum. A little farther along we note that the mucosal markings in the terminal ileum were absent. That would suggest some sort of an infiltrating process, neoplastic or inflammatory, that had eradicated those markings. The description of the mucous membrane that was noted in the x-ray examination in the cecum is further evidence but does not help in the differentiation between an inflammatory and a neoplastic process.

Are the x-ray films available?

Dr. Aubrey O. Hampton: The question of a sponge was raised and plain films were taken, but they do not show a clip such as the Massachusetts General Hospital sponges contain. Furthermore, no dilated loops of small bowel were seen, nor was there other evidence of obstruction. The film taken at the time of the barium enema shows a rather unusual picture, this being the cecum and this the terminal ileum. The terminal ileum shows definite ulceration, which ends abruptly at the margin of the mass. This smooth concave margin of the cecum represents the point of invagination into the cecum, and the mucosal folds in this area appear normal. The point at which we suspected destruction of the mucosal folds is immediately around the ileocecal valve. The abrupt ending of the process would probably help rule out ileitis or tuberculosis.

Dr. Fish: It seems to me that we have a good deal of evidence against an inflammatory process, and I might say further that a primary intussusception would hardly be considered in this situation. In the first place, for an adult to have primary intussusception is an extraordinarily rare phenomenon, and the intussusceptions that do occur are more apt to be of a type associated with chronic and intermittent low-grade obstruction of this sort. The primary lesion leading to the intussusception might be inflammatory, such as regional ileitis or tuberculosis. However, inflammatory lesions of the ileum rarely are the cause of intussusception. That leaves us with the conclusion that the primary process must have been neoplastic. Of the possible neoplastic conditions we might mention a benign neoplasm of the small bowel, but the length of involvement of the ileum is distinctly against that sort of thing. I think carcinoma is unlikely, and it seems to me that the diagnosis boils down to a lymphoma with secondary intussusception of the terminal ileum into the cecum.

Dr. William B. Breed: What about the possibility of a benign polyp associated with intussusception?

Dr. Fish: I am of the opinion that such was probably not the case, in view of Dr. Hampton's statement regarding destruction of the mucosal markings over such a length of terminal ileum.

Dr. Henry H. Faxon: There are three points of interest to bring out. In the first place, the gall-bladder incident is of interest only as it gave a chance to see what the cecum was like a relatively short time before the terminal illness. At the first operation I exposed the cecum, and am sure that nothing abnormal was present on palpation or inspection.

Secondly, the history is misleading in that it lays a good deal more emphasis on the symptom of pain than was brought out when she first came to see me. The chief thing that bothered her was the lump in the side that she herself had discovered.

The third point is that it was surprising, after the true state of affairs had been found out, she did not have more in the way of obstructive symptoms. At operation it was discovered that a large segment of the terminal ileum had intussuscepted into the cecum. Adherent to it, not by inflammatory reaction but by actual invasion of the growth, were loops of small intestine. A first-stage ileotransverse colostomy was done, and I was later able to resect the right colon and small intestine en masse. She did well immediately following operation but then developed intestinal obstruction and a fecal fistula and finally died

about ten weeks after operation, primarily from inanition because I was unable, even at a third attempt, to isolate and close this fistula.

Preoperative Diagnosis

Malignant lymphoma of terminal ileum.

Dr. Fish's Diagnoses

Lymphoma of terminal ileum.
Secondary intussusception into cecum.

Anatomic Diagnosis

Reticulum-cell sarcoma of ileum.

Pathological Discussion

Dr. Tracy B. Mallory: The differential diagnosis here was essentially that of a neoplasm that would develop as rapidly as this, assuming that the first exploration was adequate; and I think we can safely assume there was no tumor present at that time. Five months later there was a tumor of sufficient size so that the patient could feel it herself. The microscopic examination shows that it was a form of lymphoma which we classify as reticulum-cell sarcoma, a rather frequent type of lymphoma to be found in the bowel. The primary tumor was apparently in the ileum, which was most extensively involved. Besides the intussusception there was considerable neoplastic invasion of the cecum, as well as some involvement of another loop of small bowel, so a very extensive operation was necessary.

Dr. Maurice Fremont-Smith: There was no evidence of reticulum-cell sarcoma elsewhere?

Dr. Mallory: No.

Dr. J. H. Means: Was it an annular growth?

Dr. Mallory: Yes.

One question came up a few months ago in a similar case of intussusception of the ileum into the cecum. Dr. John Homans was present at the conference, and I asked him if he had ever seen intussusception in a case of regional ileitis. He said he had not. That is also our experience. We have found it quite common in association with tumors but extremely rare in association with inflammatory lesions.

Dr. Hampton: Another important point in differential diagnosis which I failed to mention was that the ileum at the site of the disease was larger than normal. In cases of regional ileitis it is small.

Dr. Fremont-Smith: Was the patient too old for a regional ileitis to occur?

Dr. Mallory: I do not believe I have seen ileitis this late in life.

CASE 26212

Presentation of Case

A thirty-six-year-old American housewife entered complaining of shortness of breath and edema.

Approximately two and a half years before admission the patient began to notice increased breathlessness on exertion, especially after climbing stairs. This dyspnea increased progressively until admission, so that she could walk only about five or ten yards on the level without becoming markedly out of breath. It had been especially marked during the past year. She stated that very often "everything went black" after the slightest exertion. Four months before entry her ankles began to become swollen toward the end of the day, but the swelling disappeared after a night's rest. During the two weeks prior to entry the swelling had become much more marked, especially on the right. During this four-month period she had been in bed practically all the time. One month before entry she noticed a swelling over the lumbar region, which appeared after she had been propped up in bed for some time; it disappeared when she lay down and reappeared when she was propped up again. Three months before admission she had had an attack of tachycardia which lasted from 6 a.m. to 1:30 p.m. and during which she had to "fight for breath." Since then she had had two or three similar attacks of a milder nature, the last one occurring about one week before entry. During the month before entry her abdomen had become distended and she felt uncomfortable when she lay on her left side. She had also had nausea and occasional vomiting. During the previous two months she had been using two pillows. Since the onset of the shortness of breath two and a half years before, she had had a dry, hacking, unproductive cough, especially following exertion; this had not changed in character.

The family history was noncontributory.

She had been married eleven years. The husband was living and well. Her first pregnancy, which had occurred ten years before entry, terminated at seven months as a result of toxemia. Two years later she had had a miscarriage at three months, and two years after that another child had died as a result of toxemia during the eighth month. Curettages had been performed four and two years before entry.

She had the usual childhood diseases. There was no history of pneumonia, pleurisy or rheumatic fever. There had been no contact with tuberculosis. She had had several severe sore throats before the age of twenty-five, and a tonsillectomy had been performed twice. Since then she had had no sore throats.

Physical examination showed a rather thin but fairly well-developed woman sitting propped up in bed and having a little difficulty in breathing and an occasional dry cough. The lips and fingertips were slightly cyanotic. The left fundus showed a bluish-gray rim about the nerve head, slightly suggesting a partial separation of the retina. The heart was greatly enlarged. The maximum apical impulse was felt 14 cm. to the left of the midsternal line in the fifth interspace, 6 cm. beyond the midclavicular line. There was no heave of the precordium, and no thrill was palpable. The sounds were loud and of good quality. The rhythm was regular. The pulmonic second sound was greater than the aortic. There was a low-pitched diastolic rumble extending through diastole and ending in a crescendo in the first sound at the apex, best heard in the axilla. A high-pitched short systolic blow and a soft systolic blow were heard over the base. The pulses were equal and of small volume. The neck veins were moderately engorged and showed visible pulsations. The blood pressure on the right was 106 systolic, 92 diastolic, and on the left 126 systolic, 118 diastolic. The chest showed dullness at both bases, with moist rales extending to the midclavicular regions. The liver was felt 9 cm. below the costal margin in the right midclavicular line, and was firm and tender. The abdomen was distended, and dull in the flanks, and a fluid wave could be demonstrated. The veins were prominent. The tip of the spleen could barely be felt. There was slight pitting edema of the feet and shins, and moderate edema of the sacrum.

The temperature was 98°F., the pulse 72, and the respirations 22.

The urine showed a specific gravity of 1.008 to 1.010, a slight trace of albumin and a sediment which contained an occasional white blood cell. The blood showed a red-cell count of 5,190,000 with a hemoglobin of 85 per cent, and a white-cell count of 13,000 with 78 per cent polymorphonuclears. The stools and sputum were normal. The venous pressure in the right arm by the direct method was 18 cm. The nonprotein nitrogen of the blood was 50 mg. per 100 cc., the serum protein 6.2 gm.

X-ray examination of the chest showed that both sides of the diaphragm were obscured by homogeneous dullness which rose in the axillary line to about the middle of the scapula. The heart shadow was difficult to outline, but the heart was enlarged both to the right and to the left. The upper left and right borders were unusually prominent. The blood vessels of the lung were large. There was extension of the dullness at the right base into the region of the interlobar pleura.

On the second day the blood pressure in the left arm was 105 systolic, 95 diastolic, and in the right, 110 systolic, 90 diastolic. Further observation showed that the heart apparently shifted several centimeters with changes from the left lateral to the right lateral position. The liver edge was felt 12 cm. below the ensiform and the same distance below the right costal border in the nipple line. There was no Broadbent sign. The patient was given 1½ gr. of digitalis three times a day. The fluid intake was limited to 1200 cc. daily. She was also given Salyrgan, without appreciable effect. She continued to cough considerably, and there was an acetone odor to the breath. Southey tubes were inserted for nine and a half hours on the twelfth day. Approximately 2000 cc. of fluid was removed. The tubes were used again about one month after entry. During the fifth week she gradually became drowsy, developed increasing pallor and showed distinctly icteric scleras. On the fortieth day, after a visit from her husband, she suddenly gasped and died in a few minutes.

Differential Diagnosis

Dr. J. Sydney Stillman: It seems clear that we are dealing here with a patient who died from heart failure. The problem is to determine as accurately as possible the nature of the pathologic changes which led to it.

The patient's history before the onset of the present illness gives some leads, but that is all. She had had two attacks of toxemia of pregnancy, leading to premature delivery in the first pregnancy and a dead baby at eight months in the third. The second pregnancy resulted in a miscarriage at three months, too early for the onset of toxemia. Two curettages, which I assume to have been therapeutic abortions, were done thereafter. The attacks of toxemia might well have led to the development of hypertension and hypertensive heart disease.

The patient had "several severe sore throats" before the age of twenty-five, apparently severe enough to lead to two tonsillectomies. There is no history of rheumatic fever, but only too frequently one finds rheumatic valvular disease without a definite history of an active rheumatic process.

The final illness began two and a half years before entry and consisted essentially of a slow, steady, progressive failure of the left heart for a little over two years; then, four months before entry, right-sided failure began. In spite of bed rest, digitalis, diuretics, restriction of fluids and Southey tubes the patient failed to rally and died on the fortieth hospital day. Unfortunately, we are not given the help of blood-pressure determi-

nations or auscultatory examinations of the heart previous to admission to the hospital.

Physical examination revealed slight orthopnea, cyanosis of the fingers and lips and an occasional dry cough. There was a suggestion of a partial separation of the left retina, probably a scar of the toxemias of pregnancy. The heart was greatly enlarged. The sounds were loud and of good quality. The rhythm was regular. The murmurs of mitral stenosis and regurgitation were present. There is a meager description of a systolic murmur at the base. The pulse pressure and systolic pressure were low, with the diastolic pressure elevated or high normal. The signs of hydrothorax and pulmonary edema are evidence of left-sided heart failure, and the cyanosis, engorged neck veins, enlarged liver and spleen, ascites and peripheral edema show marked right-sided failure.

A diagnosis of rheumatic valvular disease with mitral stenosis and regurgitation seems justified. It is hard to evaluate the systolic murmur at the base. Although it might well be caused by a slight degree of aortic stenosis, which would be supported by the decrease in intensity of the aortic second sound, it seems quite likely that it was due to a dilatation of the heart and was really a functional murmur. It does not seem necessary to have had tricuspid stenosis to account for the findings in this case, and against it are the lack of the characteristic murmurs and of pulsation of the liver. Although a subacute or chronic active rheumatic disease would lead to the relentless course this patient ran, there is no evidence to point to its existence.

Because of the marked degree of obstruction to the return of blood to the heart, the low blood and pulse pressures and the progressive course without response to the usually effective means of therapy, adhesive pericarditis must be considered. It is obvious from the statements about the shift in position of the heart with changes in position and the absence of Broadbent's sign that this diagnosis was considered by the visiting staff. In addition to the two findings just noted there are other features which make this diagnosis unlikely. First, if one accepts the diagnosis of rheumatic valvular disease, which seems advisable, the diagnosis of adhesive pericarditis is unlikely. In 15 cases of the disease reported by Dr. Paul D. White[1] and 19 cases reported by Dr. C. Sidney Burwell[2] there was no evidence that associated rheumatic heart disease or rheumatic fever played a part in the etiology. In 1000 cases of rheumatic heart disease followed at the House of the Good Samaritan there were no cases of adhesive pericarditis.[2] Furthermore, if one does not accept the diagnosis of rheumatic mitral disease one cannot explain all the murmurs. Second, the heart was larger than that found with adhesive pericarditis. Third, there was no evidence of tuberculosis, a common cause.

One must consider the possibility of hypertensive heart disease, either acting as the single cause of this patient's death or existing in conjunction with rheumatic valvular disease. The first possibility seems unlikely because of the presence of an apical diastolic murmur, the extremely large heart, the absence of any abnormally high blood-pressure reading or the history of one, the absence of vascular changes in the ocular fundi, the two-year history of progressive left-sided heart failure before the right side failed and the degree of venous obstruction.

Is it possible that the patient developed hypertension six to ten years before entry — that is, after the toxemia? It seems quite likely because she developed toxemia in the two pregnancies that lasted into the third trimester. Furthermore, Fishberg[3] says that essential hypertension develops with remarkable frequency in middle-aged women with mitral stenosis. It is possible that hypertension existed in this patient until a dilatation of the heart occurred and that the latter contributed to the marked degree of congestive failure. The high diastolic pressure and low specific gravity of the urine, with a slight trace of albumin, favor this hypothesis. However, a fall of pressure from an abnormally high level to an abnormally low one would seem more likely to have been a terminal event. The combination of mitral stenosis and hypertension frequently leads to auricular fibrillation, which this patient did not have unless the attacks of transient tachycardia were caused by paroxysmal auricular fibrillation. Furthermore, the association of these two conditions does not seem unfavorable.

In summary, I believe that this patient had rheumatic heart disease with mitral stenosis and regurgitation and possibly a slight degree of aortic stenosis. Pathologically, I should expect to find some changes in the kidneys and arterioles suggestive of essential hypertension. However, I do not believe that essential hypertension played more than a supporting role in this patient's illness. The jaundice terminally, I believe, was due to chronic passive congestion and central necrosis of the liver. I doubt the existence of true cardiac cirrhosis.

Clinical Diagnoses

Rheumatic heart disease, with mitral stenosis.
Cardiac decompensation.
Cardiac hypertrophy.

Dr. Stillman's Diagnoses

Rheumatic heart disease, with mitral stenosis and regurgitation.
Aortic stenosis, slight?
Congestive heart failure.
Chronic passive congestion of the liver, with central necrosis.
Arteriolar sclerosis.

Anatomic Diagnoses

Endocarditis, chronic rheumatic, with stenosis, mitral.
Cardiac hypertrophy, rheumatic.
Pulmonary embolus, right.
Pulmonary infarct, right lower and middle lobes.
Bronchopneumonia, right, slight.
Hydrothorax: right, marked; left, slight.

Pathological Discussion

Dr. Tracy B. Mallory: I should like to start by apologizing to Dr. Stillman for what I believe is a serious omission from the abstract of this patient's record. The initial temperature was as reported, 98°F., and subsequent recordings for the next five days ranged from 96 to 98 by mouth. As soon as a shift was made to rectal temperatures, however, it was discovered that the figures ranged constantly between 100 and 101°F., with occasional spikes to 102. She did, therefore, have a low-grade fever accompanying the leukocytosis.

Dr. Stillman was, of course, correct in his primary diagnosis of rheumatic heart disease with mitral stenosis and regurgitation. The valve leaflets were markedly thickened and interadherent, and the cords so shortened that the apices of the papillary muscles were virtually in contact with the valve margins. The other valves were negative. The heart was markedly enlarged, showing moderate hypertrophy and great dilatation of both auricles and of the right ventricle. In fact the pulmonary conus was in itself almost as large as the left ventricle. Despite the marked dilatation of the right ventricle, its wall measured 8 mm. in thickness.

This, however, was not all the story. The right pleural cavity showed, as the x-ray film suggested, a considerable amount of fluid, just under 1000 cc. In addition, however, there were two very large pulmonary infarcts, one occupying two thirds of the lower lobe, and the other almost all the middle lobe. In the corresponding branches of the pulmonary artery were grayish-red, firmly adherent thrombi, which had evidently been present for a period of some weeks. Microscopic examination of the pulmonary infarct showed a marked leukocytic reaction and beginning encapsulation at the periphery, suggesting a duration of approximately a month. Sections of lung tissue outside the areas of infarction showed considerable thickening of the small pulmonary arterioles of the type frequently seen in mitral stenosis. From the anatomical point of view the degree of cor pulmonale was greater than that which mitral stenosis alone would explain, a finding suggestive of considerable resistance within the pulmonary arterial tree itself.

We are constantly becoming more aware of the importance of pulmonary embolism in cardiac patients. Dr. White has recently called our attention to the fact that decompensation alone is not an adequate cause for fever or leukocytosis. Unsuspected pulmonary infarction is one of the factors which can frequently be shown to be responsible for such a reaction. In the diagnosis of pulmonary embolism we always lean heavily on the x-ray examination. It is worth remembering, however, that, as in this case, an accumulation of fluid may make x-ray diagnosis difficult or impossible and Hampton and Castleman[4] have shown that pleural effusion not infrequently accompanies pulmonary embolism and infarction. One point which justifiably might have aroused Dr. Stillman's suspicion was the appearance of jaundice. It is quite true that it can be explained purely on the basis of passive congestion of the liver, but it is much commoner in association with large pulmonary infarcts. Unfortunately the postmortem examination was restricted, and therefore I cannot report on the kidneys. In view of the repeated toxemias, it would have been extremely interesting to have examined them.

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LODGE MEDICAL BILL

On March 19, Senator Henry Cabot Lodge introduced a bill (S. 3630) to amend the Social Security Act. The first part of this bill provides for the furnishing of funds up to $40 per year for medical, dental and hospital services to unemployed persons who are receiving unemployment insurance benefits or to members of the families of such persons. It specifies that services of any legally practicing physician or dentist to eligible people shall be paid for, but in the case of hospitals makes a distinction between "profit" and "nonprofit" institutions. A result would be that, in the case of a doctor owning a hospital and practicing in it, the doctor could be paid for his professional services, but not for the services of his hospital. Whether this is a proper distinction, or an important one, need not be discussed. The second part of the bill provides funds for the states to match and expend, through suitable organizations, for the purpose of furnishing "x-ray treatment, respirators and certain drugs, hormones, vitamins and vaccines for the indigent." In connection with this section several parts merit discussion.

As is obvious from Senator Lodge's discussion of his bill (*Congressional Record*, 86:4702–4705, 1940), he intends that the bill provide for x-ray examination rather than x-ray treatment. He stresses that many poor people need x-ray examinations early in some illnesses, but do not secure them because of the cost. The problems that arise because x-ray examinations rather than other medical examinations are to be furnished seem interesting. Theoretically and practically the section of the public that is eligible for this aid will tend to go to the roentgenologist rather than to the general doctor, and there will be a great tendency for people to demand x-ray examinations that any doctor knows would have very little or even no chance of showing information of value to the patient.

In regard to the furnishing of drugs, Senator Lodge wants to provide especially the more expensive medicines such as insulin, which perhaps are not always available to poor people in certain areas. As a matter of fact a leading medical social worker in Boston has stated that her department has a very difficult time getting various welfare departments to furnish liver extract, insulin and so forth to many recipients of aid who need such drugs to maintain life. In the case of people not on relief rolls there is no way of obtaining such medicines except through their own efforts or the aid of private charity. This is an attempt to solve a relief problem that is theoretically correctable by intelligent administration in each local relief organization. That such provisions should be needed in any part of the country is somewhat of a reflection on these organizations.

An interesting feature of the bill is that it would take money from social-security funds and use it in the care of the indigent without regard to whether the individuals benefiting had ever contributed to the funds. Inasmuch as the social-

security funds are raised by a tax on the wages of workers and a pay-roll tax on their employers for the purpose of providing for the former in their old age, it is questionable how much of this money should be diverted to other purposes. (Such diversions are not new, but whether they are justifiable is a moot point.) If local medical care of the unemployed and indigent needs financial support from the Federal Government, and many people think it does, would it not be better to face the fact frankly and appropriate money raised by general taxes rather than take money from social-security levies? This bill in final analysis would put the Federal Government into the field of curative medicine. It would do something to alleviate two situations that have arisen only where and because local medical care for the unemployed and indigent has been either inefficient or absent. Although it is in no way comparable in size and in method of administration with the Wagner Bill, it is like the latter in taking into the province of federal administration what has always been a local function.

Why are such bills introduced? Some lay the blame to a large extent on the members of the medical profession. Who, better than they, should know the difficulties the poor have in getting good medical care and in buying lifesaving medicines? But, on the other hand, just how much has each doctor done to secure humane, efficient poor laws, to ensure the election of intelligent, honest local governments and the appointment of proper administrators and employees in welfare departments and to inform welfare departments in regard to proper methods and policies in providing the medical aspects of relief for the indigent? More individual effort along these lines is desirable and would do much in correcting a state of affairs that is at least partly responsible for the public clamor for "state medicine."

MILITARY MEDICINE

Trauma as a cause of disability is constantly growing more important with the increasing mechanization of civilization, and the surgical treatment of injury produced by physical agents is a vital factor in modern medicine. Such injuries often concern young vigorous adults not formerly a large group in the doctor's consulting room. Furthermore, the physician's activities are more and more concerned with youth and old age, and he meets those in the former group primarily for prophylactic measures against diseases that many younger physicians have only rarely seen. At no period in the world's history has medical practice so closely approximated conditions and problems formerly seen only in war time. An unusual number of articles on the treatment of individuals in the mass are written. As general health and prophylactic measures increase in number, the practicing physician is forced in increasing degree to consider problems highly similar to those of the military surgeon.

Opportunities for the study of traumatic surgery and mass public-health measures are available in highly specialized courses. Rarely are short summaries of recent advances and modern attitudes in these fields available to the practitioner of medicine. Such a course is now available in the curriculum of the Courses for Graduates at the Harvard Medical School as the course "Military Medicine and Surgery." It is open to all medical reserve officers of the United States Army and provides professional information in just those fields which are difficult for the practitioner to cover in a short time by any other means.

It is evident that the value of a well-trained medical personnel is highly important to every country. The balance of international politics is so precarious that anything may happen. Isolation from the present conflict unfortunately is not accompanied by insulation, and despite overwhelming desires, this country may become involved. If this becomes the case, it seems inevitable that a considerable military effort will be the result. Even now, the modest expansion of the Army has produced calls for reserve personnel. For doctors who hold commissions as reserve officers it becomes their duty to themselves and to the profession they represent to be, at all times, prepared for immediate efficient professional service, and for this purpose, courses such as the one here mentioned

are being conducted at various places throughout the country.

The course at the Harvard Medical School will be given during the first two weeks in June. A concise and up-to-date consideration of general problems in medicine and surgery — with particular emphasis on preventive measures, treatment and trauma — cannot fail to be advantageous. The development in these fields is sufficiently rapid to make it almost mandatory for the practitioner of medicine who is a reserve officer to take advantage of the opportunity to secure valuable postgraduate instruction.

MEDICAL EPONYM

Brodie's Abscess

Brodie's original description of the abscess bearing his name was published in 1838 or possibly somewhat later. The following quotation is taken from pages 395–411, "On Chronic Abscesses of the Tibia," in a volume, *Lectures Illustrative of Various Subjects in Pathology and Surgery* (London: Longman, Brown, Green and Longmans, 1846), by Sir Benjamin C. Brodie (1783–1862), sergeant-surgeon to the Queen. These lectures were given to the students of St. George's Hospital.

> When the tibia is enlarged from a deposit of bone externally, when there is excessive pain, such as may be supposed to depend on extreme tension, the pain being aggravated at intervals, and these symptoms continue and become still further aggravated, not yielding to medicines, or other treatment that may be had recourse to, then you may reasonably suspect the existence of abscess in the centre of the bone.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

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Pyelitis of Pregnancy

Mrs. C. M., a twenty-five-year-old primipara, when six months pregnant, entered the hospital on September 3, 1935, with a history of right-sided pain on and off for a month and a half, associated during the previous two weeks with occasional chills and fever, urgency, frequency and dysuria. She had had six days of conservative treatment in another hospital without noticeable effect.

The family history was irrelevant. The patient's past history was non-contributory. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted four days without discomfort. Her last period was March 1, making the expected date of confinement December 8.

Physical examination on admission showed a well-developed and well-nourished young woman. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. There was marked tenderness over the right kidney. The uterus was enlarged to a size consistent with the period of amenorrhea, and the fetal heart was present. A urine sediment showed large numbers of white blood cells in clumps, but no casts or red cells. A culture showed *Bacillus coli*. A blood examination on September 3 showed the hemoglobin to be 65 per cent, the red-cell count 3,920,000, and the white-cell count 24,200. A diagnosis of pyelitis was made.

On September 6 the temperature rose to 104°F. The treatment was supportive and symptomatic for nine days, but as it was thought that this treatment was of no avail and as a white-cell count on September 12 was 16,400, a cystoscopy was performed. As the urine from the right ureter contained many leukocytes, the right renal pelvis was irrigated with boric acid solution. A ureteral catheter was left in situ until September 15, when the temperature was normal.

The patient was discharged on September 21, asymptomatic. No further history on this patient could be obtained.

Comment. This case represents the scientific and rational treatment of pyelitis. A culture of the urine yielded *B. coli*. When constitutional treatment proved unavailing, the infected kidney was catheterized and irrigated and a catheter left in situ for three days, with apparent cure of this particular attack of pyelitis.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

HAY FEVER*

Hay fever is a condition in which there is an irritation of the mucous membranes or the inner linings of the nose, throat and eyelids. The defensive mechanism against an irritation of the throat is coughing, against an irritation of the eyes is tearing or watering and against one of the nose is watering and sneezing; all these are attempts to expel the mechanical irritant. If the irritant, such as a pollen granule, is composed of irritants which are capable

*A "Green Lights to Health" broadcast given by Dr. I. Chandler Walker on Tuesday, April 16, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

of being dissolved by the watery secretion of the membranes, these soluble substances prolong the symptoms already mentioned, and in addition, cause itching and local swelling of the membranes. Anybody whose membranes are irritated by soluble irritants, and these are usually proteins, is designated as sensitive or allergic to those substances.

When one is subject to symptoms of hay fever more or less continuously or spasmodically throughout the calendar year, the term perennial hay fever is used. To determine the cause of this condition a detailed and searching history as regards the symptoms is very important. Occupation, exposure to dust, gases, odors, smoke and animals, the presence of pet animals or birds in the home, exposure to face powders, shaving powders, face lotions, very fragrant perfumes, flowers and soaps, exposure to frequently repeated sudden variations in the temperature, and the ingestion of beverages and drugs, all may be causes of perennial hay fever and may be suspected from the history of the individual. Foods also are a common cause of this type of hay fever, and tests may be done in order to determine whether they are implicated.

The simplest test, called the scratch test, consists of applying small amounts of specially prepared food substances to individual slight scratches on the forearm, to which is added a liquid to dissolve the food and permit of its absorption through the broken skin. If after an interval of fifteen to thirty minutes, a small raised blister, like a mosquito bite, appears at the site of any scratch, it is concluded that the particular food which was placed on that scratch is harmful to the individual and is probably the cause of hay fever. This test is also helpful for animal hair and skin scalings, for face powders, for feathers and for pollens.

The most prevalent kind of hay fever is seasonal in type, and the symptoms are limited to one or more of the warm seasons of the year. Pollens are chiefly responsible, although the various causes which I have mentioned for perennial hay fever may be secondary to or a complication of the pollen sensitization.

Pollens are divided into two classes, namely, those that are carried by insects and those that are borne by the wind. It is the wind-borne group of pollens that cause hay fever. Another statement that is simple and nearly accurate is the following: the pollen of any tree, shrub or plant whose flower is highly scented or brightly colored rarely causes hay fever.

Here in New England we recognize three hay-fever seasons: the early spring season, during late April and May; the early summer season, extending from late May to the middle of June; and the late summer or autumn season, which begins about the middle of August and extends to the first heavy frost. During the spring season tree pollens are the cause of hay fever. The birch and oak are the worst offenders, because they shed a large quantity of pollen over a period of ten days to three weeks. The willow and poplar also shed a large quantity of pollen, but only for a period of a few days. The various grasses are the cause of the early summer type of hay fever. It is from matured grass or hay, which was first recognized as a cause of symptoms, that the term hay fever is derived. June grass which pollinates in late May often causes a short attack of hay fever. Timothy grass is the chief cause of hay fever from early June to the middle of July. Other grasses either grow too sparingly or produce too small a quantity of pollen to be considered a prominent cause of hay fever. During the autumn season, in localities north of Connecticut, we are chiefly concerned with the pollen of small-type ragweed. Pigweed, plantain and other members of this botanical family may rarely be a cause of irritation.

Treatment of the perennial type of hay fever consists primarily in the avoidance of the causative irritant. A food may be avoided, a floss or kapok pillow may be substituted for a feather pillow, a pet animal may be dispensed with, a non-irritating face powder, shaving powder or soap may be substituted for an irritating one. Where dust cannot be avoided, a mask may be worn over the nose and mouth.

A sea voyage is the only sure way of avoiding all kinds of pollens. Ragweed, however, is unknown in Europe, South America and Bermuda.

Fortunately, pollen hay fever may be treated satisfactorily. The treatment consists of a series of inoculations containing the causative pollen. After this pollen has been ascertained by skin tests, further ones are made with a series of dilutions of the pollen; these dilutions range from a strong solution of the pollen to a very weak solution. By this dilution test, it is possible to determine to what strength of pollen solution a person is sensitive; it might be considered more or less a tolerance test. This test is very important in that it determines what strength of pollen is safe to use to begin treatment. Furthermore, from this test may also be estimated the total number of treatments that are desirable.

The most generally used method of treatment is to begin inoculations about fifteen weeks prior to the usual onset of symptoms, and to give one inoculation each week up to the beginning of the pollen season. Each succeeding treatment is progressively stronger than the preceding one so that the tolerance to the pollen protein is greatly increased. The results from this method of treatment are usually excellent for the ensuing season, and if a similar series of inoculations are given for several successive years, there is a probability of permanent cure.

Overindulgence in certain foods that are closely related botanically to a pollen that causes hay fever may aggravate hay-fever symptoms during that particular pollen season. For example, the ingestion of large amounts of the cereal grains, such as white flour, by a person who is sensitive to and has hay fever from grass pollens, may increase the hay-fever symptoms. Naturally, a reduction in the quantity of the cereals taken in the diet is indicated.

Air-conditioning and air filtration of the sleeping room give a great amount of relief to those who are especially troubled at night. In fact one would have no hay fever if he spent the entire pollen season in such a room. Nasal filters are very helpful during the daytime provided all breathing is through the nose.

Sprays, various applications in the nose, and inhalers are of limited service, since the causative agents are continuously present, and the local applications are used only at intervals.

* * *

Q. Why does a person become sensitive to or allergic to something?

A. One probable reason is overexposure or overindulgence — an overstepping of one's normal tolerance. After the condition of allergy has been established in a person, he or she may transmit a similar tendency to the offspring; in other words, inheritance may play a part.

Q. How do you actually know what pollens are in the air at certain times?

A. Glass plates covered with a sticky substance are exposed to the outdoor air. Upon these plates pollen grains fall, and they may then be identified by the microscope.

Q. You mentioned the most generally employed meth-

od of treatment for hay fever: namely, to begin treatment fifteen weeks previous to the usual symptoms. What can be done for those who do not start treatment so early?

A. Inoculations may be started only a few weeks prior to the season and continued during the season. Treatment given only during the season of hay fever is the least satisfactory.

Q. I have a friend who, with pollen treatment, is completely free from symptoms with the exception of a few minutes in the morning and a short time in the evening. Can you suggest any help for the morning and evening symptoms?

A. The sudden change in the temperature to which the scantily clothed body is exposed, namely, the change from a warm bed to the cool air on arising, and from the heat of the day to the cool, damp air after sunset, may be a cause. A sudden chilling of the exposed parts of the body causes a reaction in the nose especially and in the eyes sympathetically. Less exposure in the morning and more clothing in the evening are the answers.

Q. I have heard of as many as one hundred and fifty tests being done on an allergic patient. Are as many as that necessary?

A. No, and furthermore the great majority of that number are impractical. A careful history taken by the physician will exclude many useless tests and will often suggest probable causes. At the most, thirty to forty-five tests, all of which may be done at one visit, are sufficient. For seasonal hay fever, only a few tests are necessary.

Q. Is it possible for all skin tests to be negative with a person who has hay fever throughout the year?

A. Frequently repeated head colds, a chronic infection or inflammation of the nose or sinuses is often not distinguished from perennial hay fever by the laity, although a proper diagnosis can be made by the physician. In such a case, skin tests are negative because the condition is not caused by ordinary proteins, but more probably by those of bacteria. When all other methods of treatment have failed, a course of treatments with an appropriate vaccine is often of value.

Q. You mentioned occupation as playing a part in the cause of hay fever. Will you cite a few cases?

A. Bakers frequently become sensitive to the flour dust of the cereal grains; also, escaping gas from the ovens may irritate the nose. Housewives who do considerable baking may become sensitive to flour dust. Soap powders and house dust frequently irritate the nose. Those who work in factories where, of necessity, there is much dust or lint in the air sometimes develop irritable membranes. The installation of air filtration, blowers and exhaust fans have greatly eliminated the dust problem in factories.

Q. Do roses really cause hay fever, and what is a rose cold?

A. From a practical standpoint roses do not cause hay fever. It is possible for cut roses indoors to become so dried up that the pollen will get into the air, and in unusual cases this results in an attack of hay fever that lasts for only a few hours. The fragrance of any highly scented flower may irritate the noses of some individuals, but this is not true hay fever. Out of doors, other pollens to which a person is sensitive may be deposited by air currents on the rose flower. In such a case when a person smells the rose he is inhaling some other pollen that is the actual hay-fever cause, but the rose is naturally, though wrongly, incriminated. Before it was established that grass pollen is the actual cause of hay fever at this season, roses were blamed and the condition was called rose cold.

Q. You have said that brightly colored and very fragrant flowers as a rule do not cause hay fever. The assumption, then, that goldenrod, lilacs, Easter lilies and so forth cause hay fever is erroneous?

A. The pollen of goldenrod is too heavy and too sticky to blow about, the same is true of Easter lilies. If, however, these are kept indoors for a long time and allowed to become dry, the pollen will drop off and may be blown about. The fragrance of lilacs, violets, carnations and so forth may irritate the nasal membranes temporarily, but they do not cause real hay fever. The fragrance of apple and peach blossoms may irritate some noses. Practically no flowers used for cutting cause real hay fever.

DEATHS

NOBLE — Anngenette F. Noble, M.D., of Westfield, died April 30. She was in her eightieth year.

Born at Westfield, she attended the schools there and received her degree from the Woman's Medical College of Baltimore in 1893. She was a fellow of the Massachusetts Medical Society and the American Medical Association and a member of the Women's Medical Association.

A daughter, a sister, a niece and a nephew survive her.

WEINGER — Morris A. Weinger, M.D., of Lynn, died January 27. He was in his forty-second year.

Born in New York City, he attended Columbia University and received his degree from Boston University School of Medicine in 1927. He interned at Christ Hospital, Jersey City, New Jersey, and Dayton National Military Hospital. He was assistant in cystoscopy and clinical assistant at the New York Post-Graduate Medical School and Hospital, New York City, and was assistant urologist at Midtown and Harlem hospitals, New York City. He was on the staff of the Lynn Hospital at the time of his death.

Dr. Weinger was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and two children survive him.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

GILMAN — Louis L. Gilman, M.D., of Rochester, died at the Frisbie Memorial Hospital on April 12 after a short illness. He was born at Gilmanton Iron Works, September 1, 1863, the son of Andrew and Martha (Lougee) Gilman, and was graduated from the Dartmouth Medical School in 1896. Dr. Gilman was an assistant surgeon in the United States Army from 1898 to 1901; he served in the Philippines as personal physician to General Fred Funston and also saw service at Puerto Rico. Long an enthusiastic horseman, Dr. Gilman had been recently reelected president of the New Hampshire State Fair Association and had been appointed chairman of the Executive Board of the Medical Staff at the Frisbie Memorial Hospital, which was organized about two months before his death when an offer of $200,000 was accepted for a new hospital.

Dr. Gilman was a thirty-second-degree Mason and a past exalted ruler and life member of the Rochester Lodge of Elks.

He is survived by his widow, Elizabeth Gilman.

MISCELLANY

RED-CROSS DRIVE

Orders for large quantities of surgical instruments, 10 field-hospital units complete, 150 high-speed ambulances, each capable of carrying 4 stretcher cases, and 100 auxiliary hospital trucks have been placed by the American Red Cross, it is announced by Chairman Norman H. Davis. The supplies are to be given to Red Cross societies of belligerent European countries to assist them in caring for refugees and wounded.

Placement of these orders and others for essential supplies represented the first steps by the American Red Cross in expansion of war-relief activities. To finance this expansion the Red Cross, on May 10, announced a campaign to raise a war relief fund of a minimum of $10,000,000. Prior to that date all relief activities had been financed from reserve funds of the organization and such contributions as were designated for that purpose.

In announcing the campaign to raise a minimum of $10,000,000, Chairman Davis said: "Against great pressure we have delayed this appeal for funds hoping that we could, without it, finance the war relief expected of us. The great heart of America goes out to the victims of all wars. Our sympathies must not be empty expressions. We must send clothing, bedding, medications, surgical supplies. Relief must be sent as needed and not too late to be of use."

Up to the start of the campaign, the American Red Cross had spent approximately $1,500,000 of its reserves and donations in helping sister societies in war-affected nations care for the victims of hostilities. Chapters had spent an additional $350,000 in the production of some 450,000 warm knitted and sewn garments and more than 2,000,000 surgical dressings. More than 250,000 women volunteers are at work producing relief supplies.

MAINE NEWS

Recently Registered Physicians

The following physicians were licensed to practice medicine in Maine on March 13, 1940:

THROUGH EXAMINATION

C. Davis Belcher, Portland.
William Blaisdell, Bangor.
John A. Caswell, Bangor.
Clement L. Donahue, Portland.
George F. Emerson, Farmington.
Donald C. Gates, Gray.
Paul D. Giddings, Augusta.
Maximilian Hirschler, Lewiston.
John Merrick, Portland.
Rosario A. Page, Bridgeport, Connecticut.
Hans Schurman, Lewiston.
Reinhold G. E. Ulpts, White Plains, New York.
Preston J. Van Kolken, Holland, Michigan.

THROUGH RECIPROCITY

Paul V. Davis, Warrenton, Virginia.
Samson Fisher, Bristol.
John T. Guy, Portsmouth, New Hampshire.
Joseph G. Ham, Portland.
Hyman Hillstein, Mt. Desert.
Joseph P. Reath, St. David's, Pennsylvania.

New Association Members

The following physicians have been recently admitted to membership in the Maine Medical Association:

J. B. Marcotte, Lewiston.
Bernard Gagnon, Patten.
F. F. Larrabee, Washburn.
Robert B. Somerville, Presque Isle.
Joseph E. Poerter, Portland.
Alfred Oestrich, Mexico.
Alfred W. Norris, Jonesport.
Leon Nemon, Portland.

Annual Meeting of the Maine Medical Association

The program in brief for the eighty-eighth annual meeting of the Maine Medical Association to be held at the Rangeley Lakes House, Rangeley, on June 23, 24 and 25, is as follows:

SUNDAY, JUNE 23

4:30 p.m. First meeting of the House of Delegates.
8:30 p.m. Entertainment for the doctors and their wives.

MONDAY, JUNE 24

9:30 a.m. to 12:00 m. Group conferences.
12:30 p.m. Luncheon (tables reserved for the alumni of various medical schools and members of the Tumor Clinics).
2:00 to 4:45 p.m. Clinicopathological conference and scientific session.
5:00 p.m. Election of president-elect.
5:30 p.m. Second meeting of the House of Delegates.
7:00 p.m. Dinner and dancing.
9:00 p.m. Address by V. W. Peterson, special agent, Federal Bureau of Investigation, Boston.

TUESDAY, JUNE 25

9:30 a.m. to 12:00 m. Group conferences.
12:30 p.m. Luncheon (tables reserved for past presidents and county secretaries).
2:00 to 5:00 p.m. Scientific session.
7:00 p.m. Banquet (dress informal):
Introduction of visiting delegates and guests by President George L. Pratt, M.D.
Presentation of fifty-year service medals.
Address: Governor Lewis O. Barrows.
Address: Morris Fishbein, M.D., editor of the *Journal of the American Medical Association*, "Quackery in Medicine."

NOTES

At the annual meeting of the American Surgical Association, recently held at Washington University, St. Louis, Dr. David Cheever, associate professor of surgery, Harvard Medical School, was elected president for the ensuing year.

Dr. J. H. Means, Jackson Professor of Clinical Medicine, Harvard Medical School, was elected vice-president of the Association of American Physicians during the recent annual meeting at Atlantic City.

At the annual meeting of the Austen Riggs Foundation, Incorporated, held in Stockbridge, Massachusetts, on May 11, Dr. Horace K. Richardson was elected medical director, succeeding Dr. Austen F. Riggs, who died on March 5. Dr. Robert B. Hiden was elected senior assistant medical director, and Dr. Charles H. Kimberly, junior assistant medical director.

CORRESPONDENCE

APPROVED SCHOOLS FOR LABORATORY TECHNICIANS

To the Editor: I have recently seen in the *Journal of the American Medical Association* (**114**:1269, 1940) and in the *American Journal of Clinical Pathology* (**10**:261, 1940) that an unauthorized individual in New Jersey is circularizing the medical laboratory technicians of New England asking them to join an irresponsible body, calling itself the American Medical Technologists.

As New England appears to be fertile ground for such unauthorized activities, I suggest that those concerned in the matter refer to the article in the *Journal of the American Medical Association,* which justly points out the dangers of the efforts of such an organization to destroy the educational and clinical standards that have been created by the American Medical Association and the American Society of Clinical Pathologists for the practice of this vocation.

SIDNEY C. DALRYMPLE, M.D., *Pathologist.*

Newton Hospital,
Newton Lower Falls, Massachusetts.

TUBERCULIN TEST

To the Editor: Will you kindly publish the following note in regard to change in instructions to accompany Old Tuberculin distributed by the Massachusetts Department of Public Health:

> In the revised instructions which will accompany the Old Tuberculin supplied by the Department of Public Health for tuberculin testing, suggestion is made that the test should be read in seventy-two hours rather than in forty-eight hours, as previously recommended.
>
> Many years' experience with the tuberculin test has established two reasons for this practice: first, to avoid reading a pseudoreaction due to redness alone; second, to make it possible to observe occasional delayed reactions.
>
> The criterion for a positive test is an area of edema at least 5 mm. in the broadest diameter, in addition to erythema or redness. Redness (from trauma or irritation) occurs early and disappears promptly, usually in forty-eight hours. Edema, on the other hand, when present persists for many days. In a seventy-two-hour reading of the test the edema will still be present when the redness has entirely disappeared.
>
> The seventy-two-hour reading is particularly desirable when the 1-mg. dose is used to retest children who fail to react to the first injection of .01 mg. of Old Tuberculin.

PAUL J. JAKMAUH, M.D.,
Commissioner of Public Health.

State House, Boston.

MEDICAL OFFICER, NATIONAL GUARD

To the Editor: There is a vacancy as first lieutenant in the Medical Department Detachment of the 110th Cavalry, Massachusetts National Guard. Any graduate of a Grade A medical school below the age of thirty-five and in good physical condition may apply. Since this regiment leaves for its maneuvers in June, those who are interested should make an early application. Further information may be obtained from my office.

DAVID B. STEARNS, M.D., *Commanding Officer,*
Medical Department Detachment, 110th Cavalry.

416 Marlboro Street,
Boston.

REPORTS OF MEETINGS

GREATER BOSTON MEDICAL SOCIETY

A regular meeting of the Greater Boston Medical Society was held at the Beth Israel Hospital on February 6, 1940, with Dr. Max Ritvo presiding. The first paper was by Dr. Herbert I. Harris on "Group Psychotherapy." After a short résumé of the history of the movement from Déjerine in 1904, the speaker went on to the purposes and aims of group therapy at the Pratt Clinic. It has been found that psychoneurotics are inclined to be obstinate, especially in the hands of the general physician or of the specialist in a large clinic; the one prerequisite of their successful treatment is the long time necessary for each patient, which these men are unable to afford. The group method of psychotherapy was conceived, therefore, as an effective filter that would adequately take care of the less severe cases and refer the refractive patients to a special psychiatrist.

The technic employed at the Pratt Clinic was described as childish in its appeal, thus imitating the usual responses of such patients. Several classes are held each week and any new members are given front-row seats, where they command some attention. Older members are urged to make friends with these novices, and thus an increase in social intercourse is afforded both patients. Each person is assigned a definite number in order to inflate the ego, and all old members of the group hand in an anonymous record of their progress which is read aloud. These reports are placed in three piles according to their progress and the large preponderance showing great improvement was described as a great encouragement to doubtful new members.

Dr. Harris stated that one of the most important concepts employed is that these people are really suffering and that their pains are not just imaginary. The patients are urged to attain true muscular relaxation as an antidote for their existing tension.

The results of group psychotherapy at the Pratt Clinic during the past eighteen months were reported as promising. Of all the patients admitted to the medical clinics, 26 per cent were referred to the psychiatric clinic. Of the new members of the group, more than a third claimed improvement after the first treatment, while over a half showed eventual complete disappearance of symptoms. Sixty-eight per cent of all patients treated under the system were judged to have displayed marked to complete improvement. The best results are obtained in psychoneurotic patients, with some hope being held out for those who are psychotic and schizophrenic.

The next paper was presented by Dr. William M. Shedden on "Cancer of the Rectum." The speaker made a plea for early and accurate diagnosis of existing carcinoma and for adequate treatment of precancerous lesions when found. The need for extensive operation was considered to be the direct outgrowth of the late appearance at the clinic of 60 per cent of all such lesions. In the light of Dukes's work, on the other hand, resection and colostomy were judged to be the safest procedure where palpation of the lymph nodes, even at operation, may car-

ry over a 60 per cent error. Dr. Shedden also favored Dukes's method of gradation based on the degree of penetration of the bowel and surrounding structures.

Reasons cited for wrong diagnosis and delay of treatment included ignorance of anything more than "piles" among clinic patients, fear of lost time from work, and failure of the doctor to look for serious causes of symptoms in the presence of existing hemorrhoids, adenomas or fissures. Dr. Shedden suggested routine rectal examinations in all patients as a means of discovering asymptomatic lesions, and also the possibility of routine barium enemas if the cost could be sufficiently decreased. It has been claimed by some surgeons that a properly performed digital examination will reveal any rectal lesion except those high in the sigmoid.

The reasons for delay, which amounted to more than four months in 63 per cent of the patients studied, were varied. Thirty-eight per cent had hemorrhoids, and 10 per cent had been treated for these prior to admission. Almost two thirds of the people remained well nourished, and some were even obese. Many had relief of constipation by mineral oil and a few had negative barium enemas. The presence of a soft polyp was not inconsistent with malignancy and even metastases, while an improperly performed biopsy might well be returned as negative. Dr. Shedden concluded from these findings that the opportunities for increasing the number of cures of carcinoma of the rectum rest with the local physician rather than with the surgeon who finally performs the operation.

Results at the Boston Dispensary revealed that these lesions were operable in 76 per cent of cases, and curable in 50 per cent, with a mortality of about 8 per cent.

The next presentation was by Dr. S. J. Thannhauser, who discussed "Hyperlipemia." It was noted that although Spinoza recognized "milky blood," the phenomenon was not rediscovered until 1800. And although the finding is now usually considered in association with diabetes, Dr. Thannhauser pointed out that newer partition methods indicate that some degree of hyperlipemia is far from a rarity. The speaker stated, however, that the finding of various lipids in the circulating blood was merely a reflection of changes in the organs and not necessarily an indication of metabolism.

The various causes of hyperlipemia were then briefly considered. The alimentary type, which may result in a 100 per cent increase of the fat content six hours following a meal, was not considered abnormal or significant. Dr. Thannhauser stated that a true fat migration does occur clinically but that the route of the necessary nerve stimuli is not certain. It seems to originate in starved tissue and the resulting hyperlipemia is consequently found in anemia, cachexia and so forth. A third type is found in abnormal fat deposition, which may occur in hypothyroidism and idiopathic familial lipemia. In the former case, all fats are increased, while the latter shows an elevation of only the neutral fats and an enlarged liver and spleen.

A fourth form of hyperlipemia occurs in abnormal fat and carbohydrate metabolism, such as diabetes and von Gierke's disease. Dr. Thannhauser was of the opinion that the persistence of this condition after diabetes is controlled is due to chronic pancreatitis, which may then cause the leading symptoms. The final cause of hyperlipemia cited by the speaker was a disturbance of the intracellular metabolism of the liver and spleen, such as is found in nephrosis, xanthomatosis and Gaucher's and Niemann-Pick's diseases. An increase of the total lipids is found only in nephrosis and occasionally in Niemann-Pick's disease, whereas only lecithin and cholesterol are elevated in xanthomatosis and there is a decrease of the total lipids in Gaucher's disease.

The next speaker was Dr. Samuel Proger whose subject was "Anorexia Nervosa or Hypopituitarism." Three such cases have been observed at the Boston Dispensary for periods varying from five to eight years. They all showed certain of the characteristic signs and symptoms of anorexia, insomnia, loss of weight, amenorrhea, slow pulse, low blood pressure and low basal metabolic rate. The return to normal was spontaneous in two cases, and coincident with the institution of insulin therapy in the third. Hormonal and psychotherapy proved ineffective.

Two patients returned after ostensible cure with unexplained edema of the lower extremities, while the third patient's course was complicated by generalized decalcification with spontaneous fractures.

The problem brought up by Dr. Proger was whether the condition was a neurosis or a functional hypopituitarism. The effectiveness of psychotherapy in certain cases would be difficult to explain on the latter basis. Furthermore, the whole syndrome is explainable on the basis of a voluntary anorexia following an emotional disturbance which soon becomes involuntary and leads to starvation, which can explain all the findings in this condition. It was hypothecated that anorexia in such personalities may be analogous to excessive drink in certain other people as a release mechanism.

The final paper of the evening by Dr. Ethan Allan Brown was entitled "What We Can and Cannot Do in Allergy." The speaker chose to limit his remarks to common allergic conditions which he listed in the order of their showing skin tests as follows: hay fever, asthma, eczema, urticaria and migraine. Dr. Brown stated that the lower incidence in the latter conditions merely means fewer cases are allergic, not that all such cases are less allergic. Also, the presence of these latter diseases in known allergic patients usually indicates that there are multiple sensitivities.

Hay fever was found to be 90 to 95 per cent allergic, and treatment produced the best results in that group. Fifteen per cent received complete relief in the first year, and 30 per cent after two years, but the curve then leveled off rapidly. Dr. Brown, however, advocated perennial treatment of known allergic patients, for in that way more can be learned of secondary inciting factors and desensitization can thus be enhanced. Only about 15 per cent of patients received no relief.

In asthma patients true allergy was found to play a less important role while secondary factors, both physical and emotional, were indirectly proportional to the success of treatment. Since therapy should be directed at the psyche as well as at the organic disease, Dr. Brown stressed the importance of preventing rather than curing attacks, thus preventing anxiety. The use of enteric-coated pills of epinephrine to ward off early morning episodes was described.

In regard to eczema, the speaker reminded his audience that many of the symptoms were the result of secondary dermatitis and infection. He suggested that intensive treatment of the local condition in those without proved allergy, which contains 40 per cent of this group, may result in permanent rather than temporary relief. Such diligent therapy should be continued for four to six weeks after the skin is superficially well.

Less than 20 per cent of patients suffering from urticaria were found to be allergic, and Dr. Brown therefore urged the use of psychotherapy where emotional factors play a role. The speaker emphasized that people are prone to blame the obvious rather than the possible true

cause of such eruptions. He has never found hives from strawberries and has never obtained a positive skin test in such alleged sensitivities. In the case of migraine, specific prophylaxis and desensitization are efficacious in the small percentage of cases exhibiting demonstrable allergy, but the therapy of the others has been found unsatisfactory.

NEW ENGLAND PEDIATRIC SOCIETY

On February 7, the New England Pediatric Society held a symposium at Longwood Towers, Brookline, on the treatment of meningitis. The first speaker was Dr. Josephine B. Neal, of New York City, who discussed "The Treatment of Epidemic and Streptococcal Meningitis." Dr. Neal mentioned that the results of all serum treatment have been confused in the past by the lack of an adequate means of standardization, particularly with the introduction of a new method. Further confusion of evaluation results from the variation in the type of the disease, which may be primarily septicemic or in the meninges, and also from the introduction of antitoxins which may have some antibacterial action.

In a large series of cases of meningitis, the etiologic agents in the order of their incidence were meningococci, pneumococci and streptococci. The epidemic form was found most frequently during the first year of life.

In regard to therapy of meningococcal meningitis, Dr. Neal advised the combination of drug and serum treatment rather than the use of serum or drug alone. Serum should be given intraspinously where there is no septicemia, and should be continued until two successive cerebrospinal-fluid cultures are negative. In case of clotting, ventricular rather than cisternal puncture was considered the safer procedure. In patients with septicemia, 25 to 50 cc. of serum intravenously twice a day was suggested, but this route was advocated only as a supplement to intraspinous therapy.

Although most cases responded to drug therapy, some strains have proved to be drug fast. Therefore, in drug-treated cases, serum should be given if no response is noted within a short time. Sulfapyridine, although somewhat more irregular in its action, has seemed more promising, according to early studies, than sulfanilamide. Dr. Neal reported a case fatality of 27.4 per cent for all her hospital cases, which often included very late ones.

In the treatment of streptococcal meningitis, chemotherapy has produced a drop in mortality to 28.3 per cent. Dr. Neal recommended the use of Neoprontosil rather than sulfanilamide, for it can be used intramuscularly and is efficient in lower concentrations. Therapy should be continued for at least one week even when the course is favorable, and lumbar punctures should be carried out routinely for their therapeutic effect and in order to obtain cultures. The usual careful supportive regimen was suggested, in addition to transfusions, as indicated by regular blood studies.

Dr. LeRoy Fothergill spoke on "The Treatment of Influenzal Meningitis." The increased incidence of this form of the disease, which has raised it to first place at the Children's Hospital, was emphasized by the speaker. It occurs most commonly between the ages of two months and two and a half years, when the circulating antibodies have been shown to be minimal. Prior to that time natural antibodies are present, whereas the infant's own immunity, as a result of repeated slight exposure, does not reach adequate levels until the third year.

Haemophilus influenzae is a group consisting of many heterogenous organisms, of which those causing meningitis are usually homogeneous. For the manufacture of effective antiserum it is necessary to employ virulent strains, and the isolation and crystallization of the specific polysaccharide give hope of a more potent serum, the speaker indicated.

The mechanism by which serum exerts its action in influenzal meningitis differs from the usual form in that destruction results from lysis by antibody and specific complement rather than from phagocytosis. This has practical applications, for it was recommended that complement be of the human variety and that this ingredient always be injected intraspinously to compensate for the normal absence of complement in the cerebrospinal fluid.

Dr. Fothergill suggested the use of one or two intravenous injections of serum to counteract bacteremia, and the use of serum and specific complement intrathecally. He stated that drugs had been used in addition, but that so far no improvement had resulted. Reduction in mortality has progressed from almost 100 per cent before serum to 84 per cent with the original serum and to 75 per cent with the improved serum made from virulent bacteria. The speaker quoted 6 recoveries in 12 cases treated by Alexander, who has been using rabbit rather than horse serum.

An interesting "washing" experiment was cited by Dr. Fothergill as a possible explanation of the failure to lower the mortality more substantially. This indicated that *H. influenzae* may survive intracellularly and so resist destruction. The sugar content of the spinal fluid was suggested as a good prognostic sign.

The final paper of the evening was by Dr. Maxwell Finland, who spoke on the "Treatment of Pneumococcal Meningitis." This agent is the commonest cause of meningitis in adults and is second in importance in children. Trauma was found an important predisposing factor at the Boston City Hospital, being surpassed in importance only by infections of the upper respiratory tract, paranasal sinuses and middle ears.

Dr. Finland pointed out that in this disease adequate phagocytes, besides specific antibodies and complement, are necessary for destruction of the bacteria. Sulfanilamide alone has been shown to inhibit growth of the pneumococcus, clear a low-grade bacteremia and decrease, without eliminating, the meningeal infection. The addition of specific antiserum, however, sterilizes the blood stream and meninges. The speaker stated that when serum is used in conjunction with chemotherapy only a small amount of antibody and complement are necessary, except where there is evidence of a local abscess or pneumococcal endocarditis.

Dr. Finland pointed out that the types of pneumococcus usually found are those of the nasopharyngeal flora, with Type 3 predominating. In this form of meningitis there are unusually large numbers of bacteria and tremendous amounts of specific soluble substance. On the other hand, complement is only rarely present and will rapidly disappear if introduced. Furthermore, there are no "natural" cerebrospinal antibodies, and those introduced intravenously do not reach this space.

Experiments cited by the speaker showed that despite an adequate concentration of sulfapyridine, pneumococci continue to increase for forty-eight hours. Then there is a subsequent killing off of bacteria, even in the absence of demonstrable antibodies. This occurs only with susceptible strains, a fact which cannot be ascertained beforehand. It was concluded that the combination of chemotherapy and specific antiserum was the best method of treating pneumococcal meningitis.

The technic employed at the Boston City Hospital consists in the drainage and immediate culture of the cerebro-

spinal fluid. Large doses of sulfapyridine are administered and intravenous serum injected. Intrathecally, one should inject either the patient's own serum or specific pneumococcus antiserum and complement. Sufficient fluids should be administered to ensure cerebrospinal fluid for drainage, and lumbar punctures should be performed frequently until normal. The drug is continued for at least seven to ten days, and transfusions should be given whenever indicated.

Twenty-one per cent of all cases treated with chemotherapy at the Boston City Hospital in the past three and a half years have recovered. Comparison of various combinations of therapy indicated that the use of drugs and serum is necessary in many cases of pneumococcal meningitis, and should therefore be used in all cases until more is known of the mechanism of action. Combined therapy in a small group resulted in the survival of 47 per cent.

In discussing the papers, Dr. Kenneth D. Blackfan suggested that more attention should be focused on the entire patient until additional advances are made in specific therapy. He warned of the comparison of statistics gleaned from seasons when the virulence of the organism and the resistance of the host are variable. The importance of early diagnosis was stressed, and its difficulty alluded to, particularly in children.

NOTICES

TRUDEAU SOCIETY OF BOSTON

A meeting of the Trudeau Society of Boston will be held at the Bristol County Tuberculosis Sanatorium, Attleboro, Massachusetts, on Tuesday, May 28, at 4:00 p.m.

PROGRAM

The Role of Atelectasis in Pulmonary Tuberculosis. Dr. Felix Fleischner.

Presentation of Cases.

- Cases illustrating problems in management. Dr. Garnett P. Smith.
- Follow-up cases of bilateral disease in an adolescent. Dr. P. E. Johnson.
- Two cases illustrating extrapleural pneumothorax. Dr. R. H. Betts.
- Cases illustrating lack of deformity following thoracoplasty. Dr. William R. Rumel.
- Discussion of case for differentiation diagnosis. Dr. Richard H. Overholt.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Salem	June 3	Harold C. Bean
Haverhill	June 5	William T. Green
Lowell	June 7	Albert H. Brewster
Gardner	June 11	Mark H. Rogers
Pittsfield	June 17	Francis A. Slowick
Northampton	June 19	Garry deN. Hough, Jr.
Brockton	June 20	George W. Van Gorder
Worcester	June 21	John W. O'Meara
Fall River	June 24	Eugene A. McCarthy
Hyannis	June 25	Paul L. Norton

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The spring meeting of the New England Obstetrical and Gynecological Society will be held at the Mary Fletcher Hospital, Burlington, Vermont, on Wednesday, June 12.

Registration and operative clinics will be held from 8:30 a.m. to 12:00 noon. Luncheon will be served at the Burlington Country Club at 1:00 p.m., and a meeting of the executive committee will be held at 1:30 p.m.

A dry clinic at the Fleming Museum will take place at 2:00 p.m. There will be a symposium on pelvic trauma and relaxations. The program will be as follows:

- Obstetrical Conservation of the Birth Canal: Episiotomy, secondary repairs and so forth. Dr. H. A. Durfee.
- Restoration of the Birth Canal: Anterior and posterior plastic operations and the Kennedy operation for urinary incontinence. Dr. B. F. Clark.
- Prevention and Treatment of Retroversion. Dr. E. D. McSweeney.
- Surgical Cure of Uterine Prolapse. Dr. O. N. Eastman.

There will be a general meeting of the society and assembly at the Burlington Country Club at 5:00 p.m. Dinner will be served at 6:00 p.m.

JEFFERSON MEDICAL COLLEGE ALUMNI ASSOCIATION

During the meeting of the American Medical Association in New York City, the Jefferson Medical College Alumni Association will hold its reunion banquet on Wednesday evening, June 12, at 7 o'clock, at the Murray Hill Hotel, Park Avenue, at 41st Street. Tickets are $2.50 each. Requests for reservations should be addressed to Dr. Thomas F. Duhigg at that hotel, but all alumni are urged to attend even though they have neglected to make reservations.

AMERICAN NEISSERIAN MEDICAL SOCIETY

The sixth annual session of the American Neisserian Medical Society will be held at the Shelton Hotel, New York City, on June 10 and 11. The program will consist of the presentation of papers on the biology of the gonococcus, vulvovaginitis and the prophylaxis, diagnosis, treatment and cure of gonococcal infection.

All who are interested are cordially invited to attend the meetings.

PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

Plans for a Pan-American Congress of Ophthalmology to be held at the Hotel Cleveland, Cleveland, Ohio, October 11 and 12, have been announced.

The congress will be sponsored by the American Academy of Ophthalmology and Otolaryngology, an organization of more than 2500 specialists in diseases of the eye, ear, nose and throat, which will hold its annual convention immediately preceding the Pan-American gathering.

The United States Department of State has expressed its interest, and the governments of all the countries of the Western Hemisphere have been invited to send official delegates. It is believed that the meeting will do much toward bringing about an *entente cordiale* among scientific men of the two Americas, and it is expected that a permanent organization will be effected.

Papers in Spanish or Portuguese will be made understandable to English-speaking ophthalmologists by the use

of lantern slides projecting a synopsis of each paragraph translated into English. The reverse process will be used with the English papers. Spanish and Portuguese stenographers will be present to record the discussions in the language of the authors.

The congress is open to any ophthalmologist who wishes to register. Individual invitations have been sent to about 1800 members of the ophthalmologic profession in the Latin-American countries, as well as to the national societies of eye specialists and the universities. Individual invitations have not been sent to ophthalmologists in the United States and Canada, but official invitations to them are being printed in the various journals of ophthalmology. A fee of $5 has been set for membership in the congress.

More detailed information may be obtained from Dr. William P. Wherry, 1500 Medical Arts Building, Omaha, Nebraska.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, May 26

Tuesday, May 28

*9–10 a.m. Personality Factors in Internal Medicine. Dr. C. Macfie Campbell. Joseph H. Pratt Diagnostic Hospital.

Wednesday, May 29

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

Friday, May 31

*9–10 a.m. Changes in the Circulation Produced by Poor Postural Adaptation. Dr. Eugene A. Stead, Jr. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

May 28 — Trudeau Society of Boston. Page 898.

June 4–6 — National Gastroenterological Association. Page 737, issue of April 25.

June 4–7 — American Association of Industrial Physicians and Surgeons. Page 654, issue of April 11.

June 7, 8 — American Heart Association. Page 469, issue of March 14.

June 7–10 — American Board of Obstetrics and Gynecology. Page 608, issue of April 4.

June 8 — Dedication of Osler Memorial. Page 862, issue of May 16.

June 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

June 8–10 — American College of Chest Physicians. Page 781, issue of May 2.

June 10 — American Medical Golfing Association. Page 824, issue of May 9.

June 10, 11 — American Neisserian Medical Society. Page 898.

June 10–14 — American Medical Association. Annual meeting, New York City.

June 10–14 — American Physicians' Art Association. Page 332, issue of February 22.

June 12 — Harvard Medical Alumni Association. Page 781, issue of May 2.

June 12 — New England Obstetrical and Gynecological Society. Page 898.

June 12 — Jefferson Medical College Alumni Association. Page 898.

June 23–25 — Maine Medical Association. Annual meeting. Rangeley Lakes.

June 25–27 — Medical Library Association. Page 862, issue of May 16.

June 27 — Pentucket Association of Physicians. The Try-Angle, Groveland.

September 2–6 — American Congress of Physical Therapy. Page 862, issue of May 16.

October 8–11 — American Public Health Association. Page 655, issue of April 11.

October 11, 12 — Pan-American Congress of Ophthalmology. Page 898.

October 21 — American Board of Internal Medicine, Inc. Page 369, issue of February 29.

District Medical Society

MIDDLESEX NORTH

July 31.

October 30.

BOOK REVIEWS

Blood Groups and Blood Transfusion. Alexander S. Wiener. Second edition. 306 pp. Springfield, Illinois, and Baltimore: Charles C Thomas, 1939. $5.00.

The second edition of this well-known work has clarified a number of subjects which were formerly not clearly understood; therefore, a good deal of new material has been added to every chapter and some of the old material has been deleted. The application of blood grouping to medicolegal work has been treated in more detail, and the section on the grouping of blood stains has been completely rewritten and expanded.

In the chapter on the technic of blood transfusions there are several points in regard to the citrate method which require correction. The author apparently approves the straining of citrated blood through gauze before injection into the patient. In the reviewer's experience, however, this has often led to clotting of the blood because of the presence of calcium salts in the bleached gauze. This is an obvious chemical reaction since calcium precipitates soluble citrates.

In ascribing to Marriott and Kekwick a citrate apparatus which is completely enclosed, the author apparently is not aware that this method was used by the United States Army Medical Corps during the World War. Furthermore, in regard to continuous drip transfusions, it should be mentioned that Marriott and Kekwick did not describe this technic until seven years after it had been in common use in certain hospitals in the United States. Fortunately, the author points to the dangers inherent in the use of preserved and "bank" blood — a warning particularly timely with the increased and sometimes uncritical enthusiasm for this technic.

As usual, the publisher and printer have done an excellent job. It is a volume which should be on the shelf of every physician.

In Memoria del Prof. Fabio Rivalta. Società Medico-Chirurgica di Romagna. 398 pp. Faenza, Italy: Fratelli Lega, 1939.

On September 18, 1938, at Cesena, Italy, the Società Medico-Chirurgica di Romagna held a meeting of commemoration for Prof. Fabio Rivalta, who had died on September 2. In connection with this meeting, the society has published a memorial volume, to which thirty-three of his students and friends have contributed articles covering all the fields of medicine. The volume also contains a good portrait, a short biography and a bibliography of his writings.

Prof. Rivalta was best known for the discovery of the so-called "Rivalta reaction" for the differentiation of transudates and inflammatory exudates, which he first described in 1910. In the memorial volume this subject is discussed in three articles by Drs. Chiodini and Gironi.

Health for New York City's Millions: An account of activities of the Department of Health of the City of New York for 1938 with comparative vital statistics tables. Edited by Savel Zimand. 295 pp. New York: Department of Health, 1939.

Dr. Rice's informative and substantial record of the activities of the Department of Health of New York City for the year 1938 is an effective answer to the criticism that records of health department activities are of necessity as dry as dust. With no sacrifice of accuracy this volume presents all the information essential to a health-

department report in an exceptionally readable form. In part the success in presentation of the material is due to the use of brief statements of the underlying plan or policy at the beginnings of chapters which lead the interest up to the facts themselves. The judicious use of photographs adds materially to the attractiveness of the book for the lay reader.

To the health officer this is an impressive record of well-balanced municipal health administration. An outstanding feature of the New York City program is the development of neighborhood health centers throughout the city. This is the most effective method yet tried for bringing health services to the people in urban communities and is indispensable in a city the size of New York. The epidemiologist may feel somewhat confused to find case rates and death rates for whooping cough based on the estimated population under five years of age, the rates for measles on the population under fifteen, and the rates for poliomyelitis on the total population. The emphasis on age susceptibility is important, but comparison becomes difficult.

To the physician such a report is a reminder of how far public health can supplement medical treatment without invading the field of practice. More than that, in such activities as the consultation chest services for physicians and the pneumococcus-typing stations, the health department is making available to the general practitioner services which he cannot readily provide for himself.

The Story of Surgery. Harvey Graham. 425 pp. New York: Doubleday, Doran & Co., Inc., 1939. $3.75.

The author of this book has assumed the pen name of Harvey Graham, and is said to be a distinguished British physician; his identity is unknown to the reviewer. His *Story of Surgery* is in many ways a remarkable and unique book. Avowedly a "story book," it is in fact a readable running narrative of the evolution of the science and art of surgery from prehistoric times to the present, told with humor and essential historical accuracy but with occasional excursions of the imagination, which fill in the factual lean spots, to the great satisfaction of anyone but a scholar. The author defines his purpose by saying that it is not a history book or historical treatise, and that it should be read by "an ordinary man or woman — as distinct from that nebulous and rather awe-inspiring creature the intelligent layman." There are no bibliographic notes, but an appended list of sixty-odd books and monographs, comprising the chief source material, and indices of names and subjects. There are twenty-three admirably executed plates, among which New England readers will be glad to see the familiar painting of the first operation under ether, at the Massachusetts General Hospital.

The stories of the greatest figures in surgery — Paré, Harvey, Hunter, Lister — are admirably told. It is perhaps in the account of contemporaneous surgery and in prognostication of the future that the author is least happy. Few will agree that "Russia is untrammelled and ahead in all the sciences of medical research" or that "diabetic gangrene is now a surgical rarity," or that the female relatives of a woman with cancer of the breast are several times more likely to develop the disease than are other women and therefore that any lump should be treated by complete mastectomy. The part played by American surgeons in modern surgical progress is by no means adequately portrayed, an example of which is the attribution to "Dr. McBurney of Roxbury" of the chief part in the evolution of the surgical treatment of appendicitis in America. Halsted's contribution was rubber gloves, and Cushing is not mentioned in connection with brain tumor.

The *Story of Surgery* may be confidently recommended as entertaining and instructive reading for doctors and for such laymen as have more than a casual interest in the subject.

Tumors of the Skin: Benign and malignant. Joseph J. Eller. 607 pp. Philadelphia: Lea & Febiger, 1939. $10.00.

This book will be valuable to medical students, physicians and dermatologists because the subject — tumors of the skin — is comprehensively discussed in one small volume. The appearance of benign and malignant new-growths is adequately described, as well as the etiology, prognosis and treatment, and a clear picture is presented in a readable manner. The chapters on carcinomas of the skin with the differentiation of the basal-cell and squamous-cell types might arouse controversy among some pathologists, but it corresponds with the opinions of many dermatologists. The diagrammatic examples of these lesions in special locations, with suggested methods of therapy in their prevention, contain many valuable and practical ideas. Radium plaques properly constructed as to size and strength have been found of more value in the treatment of various cutaneous lesions than are radium tubes, and, in the opinion of the reviewer, are more practical in the treatment of superficial tumors where superficial radiation is indicated. It is interesting and refreshing to read a book written by a dermatologist who has the courage to outline an intelligent and workable technic for cutaneous surgery, which, with proper instruction, could be and should be mastered by young men entering dermatology. The principles and technic of roentgen and radium theory are clearly expressed. There is an excellent appendix containing practically all the data on radiation, physics and biology, including dosage tables and charts.

The Vitamins: A symposium arranged under the auspices of the Council on Pharmacy and Chemistry and the Council on Foods of the American Medical Association. 637 pp. Chicago: American Medical Association, 1939. $1.50.

The achievements in the science of nutrition in recent years have been numerous as well as most significant in the realm of modern medicine. The original vitamin alphabet has been greatly extended, and some of them have been subdivided. Research in vitamins tends largely toward their isolation and synthesis. New factors have been discovered which concern the growth of animals, their prothrombin content, abortion in cattle, effects on the endocrines and a variety of physiological effects. In view of the galaxy of diverse work on vitamins, new discoveries and rapid progress, this symposium is more than welcome.

Each chapter is written by distinguished investigators in their respective fields. Clearly written and understandable, without confusing excursions in intricate details, it is recommended to all. It should be a relief to those who up to now have depended on the somewhat exaggerated interpretations expressed in the pamphlets issued by pharmaceutical houses. In the introduction Dr. Morris Fishbein warns "the public and the medical profession against the commercial exploitation of individual vitamin preparations and particularly against the promotion of mixtures of vitamins as panaceas." This volume clearly presents the clinical and laboratory aspects of vitamins and deserves unrestricted praise.

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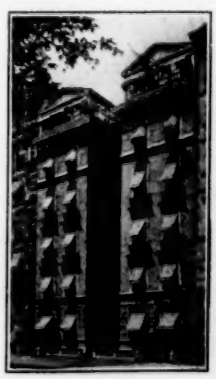

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